SCIENCE HISTORY INSTITUTE

J. THROCK WATSON

Transcript of an Interview
Conducted by

Michael Grayson

at

J. Throck Watson's home
Laingsburg, Michigan

on

27 and 28 October 2013

(With Subsequent Corrections and Additions)

ACKNOWLEDGMENT

This oral history is one in a series initiated by the Science History Institute on behalf of the American Society for Mass Spectrometry. The series documents the personal perspectives of individuals related to the advancement of mass spectrometric instrumentation, and records the human dimensions of the growth of mass spectrometry in academic, industrial, and governmental laboratories during the twentieth century.

This project is made possible through the generous support of the

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J. THROCK WATSON

1939	Born in Casey, Iowa, on 2 May

Education

1961	BS, Iowa State University, Chemistry
1965	PhD, Massachusetts Institute of Technology, Analytical Chemistry

Professional Experience

Institut de Chimie, Université de Strasbourg

1968-1969	Postdoctoral position

Vanderbilt University School of Medicine

1969-1973	Assistant Professor of Pharmacology
1973-1980	Associate Professor of Pharmacology

Michigan State University

1980-2006	Professor of Biochemistry
1980-2006	Professor of Chemistry

MSU/NIH Mass Spectrometry Facility

1980-1999	Principal Investigator and Director

Honors

1960/1961	Texaco Scholarship in Organic Chemistry, Iowa State University
1963	DuPont Teaching Fellow at MIT
1964	Minnesota Mining and Manufacturing Research Fellow, MIT
1972	Outstanding Young Alumnus, Iowa State University
1973/1977	NIH Career Development Award, Vanderbilt University
1981	Citation of Merit, Iowa State University
1990	Pittsburgh Spectroscopy Society Awardee
1992/1995	Professeur Invité, École Normale Superieure, Paris, France
1996-1999	Member, Standing Committee of National Research Council
2000	Professeur Invité, Université des Sciences et Technologies, Lille, France
2002	Professeur Invité, Université de Nice, Sophia-Antipolis, Nice, France

ABSTRACT

J. Throck Watson was born in 1939 and grew up in small towns in Iowa. His father worked at the local school, and his mother stayed at home. Watson spent much of his childhood outdoors, playing with his brother and his cousins. In the summers, he helped his father and uncle harvest bluegrass. As a senior in high school, Watson took a chemistry class and found it so fascinating that he decided to major in chemistry at Iowa State University. He participated in a fraternity and worked with Harry J. Svec, who encouraged him to attend the Massachusetts Institute of Technology (MIT) for graduate school. As a PhD student at MIT, Watson worked with Klaus Biemann on a mechanical project to use molecular effusion to remove partially the carrier gas in a combination gas chromatograph/mass spectrometer instrument. Upon graduation, Watson served three years in the US Air Force to fulfill his military commitment incurred due to his participation in ROTC during college, which was deferred during Watson's time in graduate school. He was stationed at Brooks Air Force Base in San Antonio, Texas, where he worked at the School of Aerospace Medicine. After his tour of duty was complete, Watson accepted a postdoctoral position at the Institut de Chimie, Université de Strasbourg in France where he learned practical organic mass spectrometry. At the time, the French were favorable toward the Americans, so Watson had a positive experience abroad, which reminded him of his summer job in Bavaria, Germany, during college when he worked as a farm laborer.

When the one-year postdoc ended, Watson accepted a professorship of pharmacology at Vanderbilt University where he taught pharmacology classes and worked on a book, *Introduction to Mass Spectrometry*. After gaining tenure at Vanderbilt, the director of the mass spectrometry facility at Michigan State University called Watson and told him he was stepping down and wanted Watson to take his place. Watson accepted the position on the condition that he would be part of the chemistry faculty, which was granted. At Michigan State, Watson had many graduate students. During a sabbatical, he worked with Christian Rolando in France. Of all of his contributions to science, he was most proud of his work with his graduate students at Michigan State. When a grant application was not renewed, he decided to retire and "go fishing." Watson ends the interview by discussing hydrogen ions, instrumentation, working with graduate students, grants, professional societies like the American Chemical Society and the American Society for Mass Spectrometry, analytical chemistry, various colleagues, the origin of his middle name "Throck," and the importance of his research today.

INTERVIEWER

Michael Grayson is a member of the Mass Spectrometry Research Resource at Washington University in St. Louis. He received his BS degree in physics from St. Louis University in 1963 and his MS in physics from the University of Missouri at Rolla in 1965. He is the author of over 45 papers in the scientific literature. Before joining the Research Resource, he was a staff scientist at McDonnell Douglas Research Laboratory. While completing his undergraduate and graduate education, he worked at Monsanto Company in St. Louis, where he learned the art and science of mass spectrometry. Grayson is a member of the American Society for Mass Spectrometry (ASMS), and has served many different positions within that organization. He has served on the Board of Trustees of CHF and is currently a member of CHF's Heritage Council. He currently pursues his interest in the history of mass spectrometry by

recording oral histories, assisting in the collection of papers, and researching the early history of the field.

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INTERVIEWER: **Michael A. Grayson**

LOCATION: **Watson's home**
Laingsburg, Michigan

DATE: **27 October 2013**

GRAYSON: Let me start by saying that this is October the twenty-seventh, and I'm at the residence and the farm of Dr. J. T. Watson, Jack Throck Watson, in rural Michigan to conduct an oral history of Jack and his career. Jack, I'd like to explore your early childhood influences that led you into science. So tell me a little about your parents.

WATSON: Well, I grew up in small towns in Iowa and the small town where I went to high school was Nora Springs, Iowa, population of about one thousand. My father was the school superintendent and taught advanced mathematics and physics in said high school. My mother—

GRAYSON: What was his name?

WATSON: Jesse H. Watson. He had ten siblings, eight of whom settled in Iowa within a radius of fifty miles of our house, so we had many family reunions. Virtually every weekend we would get together at one of the uncles' or aunts' house. I grew up with about ten cousins, some of whom I still hunt and fish with even today. My father had a very close eye on my performance in math and English. He insisted that I have a 3.0 in those courses, so that helped me be prepared for college, and eventually graduate school from that early emphasis on math and so forth. My mother was not in science. She was a housewife.

GRAYSON: Her name was?

WATSON: Anne Watson.

GRAYSON: And her maiden name?

WATSON: Her maiden name was Young. [. . .] She grew up in [the] Springfield, Missouri, area. And that's where my parents retired [and where they died].

GRAYSON: Nowadays if your parent was [on the faculty of your] high school it would be an embarrassment for the student. Was that the case?

WATSON: Oh well, it was tough. I couldn't be a normal kid. I was the superintendent's kid. So everyone was watching me pretty carefully. It probably was not as bad as being the preacher's son, but being superintendent's son was a little tough. And I had him as an instructor in physics and in algebra, and he had a rule that I couldn't get an A on any exam unless at least one other student did the equivalent. And I'm sure he told **<T: 05 min>** his faculty to not ease up on me. I mean, I got as many whippings by other faculty members as normal kids. I guess that's where I was normal. [laughter]

GRAYSON: So when you say whippings are you talking about physical whippings or—

WATSON: Physical whippings. Like throwing food in the lunchroom, the shop teacher took us down to the shop and said okay, and there was this big stack of lumber there and he says, "Choose your paddle." [laughter]

GRAYSON: Can't get away with that today.

WATSON: [Yes], my dad was a believer in corporal punishment and instilled that in the school. He made a point out of hiring male faculty. So it was a tough group of guys, good discipline.

GRAYSON: Well, it sounds like he kept you guys in line pretty well.

WATSON: Indeed.

GRAYSON: What about their parents? Did they have any—

WATSON: On my father's lineage there were a lot of schoolteachers, and so he, sort of, fit into that pattern, I guess, but took an interest somehow in school administration, got a master's in School Administration, which I guess officially helped him get prepared to be the superintendent of schools.

GRAYSON: And your mom's background?

WATSON: My mother grew up on a farm in Western Kansas and then eventually [moved] into Missouri. Her family was in the orchard business: apples, peaches and fruit, in fact, of course . . .

GRAYSON: Now did you have any siblings?

WATSON: I have one brother who suffered the same—

GRAYSON: Upbringing?

WATSON: Upbringing as I with regards to school. He too was to do well in math and English. He became an aeronautical engineer and, you know, I went into chemistry.

GRAYSON: Is he older or younger?

WATSON: He's younger than I.

GRAYSON: And his name is?

WATSON: His name is George. George Huston Watson. My father's name was Jesse Huston Watson, by the way. So Huston was a common and important name in our family.

GRAYSON: [. . .] So basically you really had a fairly strong basic education and family emphasis was on getting a good education. So it was not an option. You really had to do that?

WATSON: [Yes], I was going [to] go to college. [. . .]

GRAYSON: Now I noticed one thing that's pretty obvious from just my short brief period here and knowing you previously is that you seem to be very much interested in the outdoors: hunting, natural wildlife and so on. So that's been a large part of your life. When did that start?

WATSON: Well, that happened effectively with the large extended family of my father's brothers and sisters living nearby and of course all the cousins. We would do pheasant hunting as a group, and I grew up in Northern Iowa, which of course means we're close to Minnesota, and we spent many family trips in Minnesota fishing as a family, so those bonds were established early on.

GRAYSON: So this is at a very young age, I would imagine.

WATSON: [Yes], and I think anywhere from age of six, seven on up through teenager.

GRAYSON: So was your dad involved in this activity of hunting? **<T: 10 min>**

WATSON: [Yes,] and his brothers and brother-in-law.

GRAYSON: So that's really a major theme in your career, so to speak, being close to nature.

WATSON: [Yes.] Another interesting aspect was that my father and his brother-in-law got into the bluegrass harvest. Bluegrass is what grows in most lawns and on golf courses, and in Iowa bluegrass grows naturally in cow pastures. So it was a common activity during the summer that we would use a fleet of Willy jeeps—the kind that were used in World War II—and tractors to pull bluegrass strippers through the cow pastures. These were machines that ostensibly were designed for the purpose of knocking the seeds out of the seed pods in the mature bluegrass without removing the leaves and the stock of the bluegrass plant. So we would go into a farmer's pasture, harvest the seed selectively with these bluegrass strippers, strip the seeds, so to speak, leaving behind enough of the bluegrass plants that the farmer could continue to graze the pastures. This was a fairly good source of income for a schoolteacher who wasn't making all that much and for me it became income that eventually paid for my college education and also helped on into graduate school.

GRAYSON: So this was strictly a summer job?

WATSON: That's right. It was summer.

GRAYSON: And does that work well with your dad's a—

WATSON: A schoolteacher, [yes].

GRAYSON: Were there any other teachers at your high school who influenced you in any way? Because I mean obviously your father had a strong influence but—

WATSON: Yes, well, it was very interesting. It was a small high school. The city of Nora Springs had a population of one thousand, and the high school had only a little over one hundred students and, in my class, twenty-five students. There were pretty good courses given—advanced math, algebra, trigonometry, and so forth—but there was no chemistry in the high school.

The year I was a senior they made the bold move of establishing a chemistry course. At least, that was the idea. The trouble was that they didn't have a chemistry teacher. As it turned out the English teacher had taken a chemistry course somewhere in his past which rendered him the candidate for teaching the course in chemistry, and I told my dad I didn't want to take that course. He said, "Well, why not?" And I said, "Well, I don't want to be a chemist. I don't want to be running around in a white coat like a Volkswagen mechanic." And he said, "Well, it's okay if you don't like chemistry, but you need to take the course to figure out whether you do like it."

And I figured that was a pretty good argument and so I took the chemistry course and found it fascinating. Prior to that because I was pretty good in math, I was, sort of, headed in the direction of becoming a CPA [certified public accountant] because I was good with numbers. Thank goodness that didn't come to fruition. **<T: 15 min>** It was very clear to me even before the year's end of the chemistry course that I wanted to go into chemistry and that's in fact what I did at Iowa State University which was renowned for its excellence in science and engineering.

GRAYSON: This is a land grant college?[1]

WATSON: That was a land grant college: Iowa State University at Ames, Iowa. So interestingly enough it was an English teacher that influenced me heavily into going into chemistry. [laughter]

GRAYSON: So did he—

[1] The 1862 Morrill Act allowed states to fund colleges by selling federal land. Founded in 1862, Iowa State University was the first college established through the Morrill Act.

WATSON: And my dad said that the reason that he assigned him to the chemistry course was he was a good salesman. So I guess he sold me . . . the English teacher sold me on the field of chemistry.

GRAYSON: I was just curious if he really was able to convey the material to you in his lectures, or did you have to rely on the book? Or obviously he did something to make it interesting.

WATSON: He certainly, you know, went by the book. He had no practical experience in chemistry, but he did some experiments. I remember some that made me pretty nervous, the one with sulfuric acid and sodium bicarbonate which sprayed some sulfuric acid over several members of the class. Thankfully no one was injured. Some people got holes burned in their clothes but no injuries thankfully.

GRAYSON: Well, it's a testament to his teaching ability, I guess.

WATSON: Indeed. Well, I can . . . my dad said he was a good salesman. [laughter]

GRAYSON: So you decided actually when you entered Iowa State that chemistry was going to be your major?

WATSON: Well, in fact I went to Iowa State undecided as to whether I was going to pursue chemistry or whether I was going to pursue chemical engineering. And as it turned out there was a program at Iowa State at that time that was effectively a double major—chemistry and chemical engineering—and I took that route. So I took engineering physics and, of course, the chemical engineering hardware course.

GRAYSON: So you had a pretty broad . . . . This is a four-year program?

WATSON: Yes.

GRAYSON: So [. . .] that was pretty intense.

WATSON: It was, [yes]. I'll tell you, the second year at Iowa State was a killer, and I was in a fraternity. In fact I eventually became president of the fraternity and—

GRAYSON: What's the name of the fraternity?

WATSON: Theta Xi Fraternity [. . .] As a sophomore I was taking organic chemistry, engineering, chemical engineering, differential equations and that sort of thing. I remember the organic chemistry course lectures were Tuesday, Thursday, and Saturday. So Friday night when my fraternity brothers were wanting to go out, double-date, I was getting ready for organic chemistry lecture the following morning. Not a fun time. [laughter]

GRAYSON: But you were dedicated to doing what was required to get a good grade in the course.

WATSON: That's true.

GRAYSON: So were there any instructors that were particularly inspiring to when you were in your college at Iowa State?

WATSON: Well, that's interesting. I took a special project in my undergraduate days with Harry [J.] Svec who was a professor of physical chemistry. **<T: 20 min>** I did a special project on determining the charge on an electron using the Millikan oil drop experiment. Svec was fairly impressed with my result of that special project. He was most influential in directing me toward MIT [Massachusetts Institute of Technology], and I think it was probably his recommendation that helped me get in there. But the other interesting thing that I learned when I got to Iowa State was that I did not have the usual path into chemistry. Most of my classmates at Iowa State—these were classes of two hundred students, I suppose—most of those students had gotten into chemistry in grade school by using chemistry sets. I had never even seen one and also most of my classmates were advanced, came to Iowa State advanced placed out of high school in chemistry and, of course, my English teacher for chemistry didn't offer the advanced placement. So I felt a little inadequate but I managed to survive with hard work.

GRAYSON: So besides Svec were there any other teachers there that—

WATSON: No, not particularly. I learned early on that organic chemistry was not one of my favorites.

GRAYSON: Was not?

WATSON: Was not a favorite course of mine.

GRAYSON: I can't understand why not.

WATSON: [Yes], Saturday morning classes probably had something to do with it.

GRAYSON: But after your sophomore year, that's when you were done with organic chemistry, I think.

WATSON: [Yes], that's true.

GRAYSON: Of course P-Chem [physical chemistry] can be a bit of a challenge.

WATSON: [Yes], P-Chem was tough.

GRAYSON: So you probably followed a pretty intense development of your chemistry knowledge in this period and you say that Svec really influenced you with regard to going on to graduate school or was it something you toyed with?

WATSON: Yes, Svec directed me to apply to graduate school institutions of renown which I surely wouldn't have done on my own. In fact when I got accepted to MIT, I was quite concerned because at that point I sort of realized that I really didn't know anything in chemistry and that I needed to study. So I spent the summer before I went to MIT reviewing all my coursework in chemistry which helped me when I got to MIT—helped me qualify in the areas of analytical, physical and organic and so forth, the normal process. But as I had feared I found myself among peers who were extraordinarily intelligent and that both worried me, frightened me to some extent. But in the end the most rewarding aspect of going to graduate school was the extremely high level of achievement and intelligence of my classmates.

GRAYSON: So if Svec hadn't interfered or **<T: 25 min>** interceded, you probably . . . would you on your own have thought about going to graduate school?

WATSON: I would have because I realized I didn't know anything. I realized as I was interviewing for industrial jobs. I realized, for example, I didn't know anything about EMR [electromagnetic radiation] and I knew that I needed much more study and my classmates were going to graduate school so that was a natural thing to consider.

GRAYSON: So it was something that you would have probably pursued without Svec but he—

WATSON: I think so. I think in general I would have done that but—

GRAYSON: And he pointed you in a specific—

WATSON: I think he suggestively guided me, anyway, to MIT.

GRAYSON: What other schools . . . did you recall any other graduate school?

WATSON: I applied and was accepted at the University of Michigan. Ironically, I joined the faculty eventually at Michigan State University, the arch-rival of the University of Michigan. But I applied to Penn State [Pennsylvania State University], University of Pennsylvania, as I recall. I possibly applied to Berkeley [University of California, Berkeley] but I don't remember.

GRAYSON: But you opted for MIT?

WATSON: I did. I think I also did some silly things like apply to the University of Florida because I was tired of walking through slush to class—silly things like that. I think that's where Svec stepped in and said, "You need to give this some serious thought." [laughter]

GRAYSON: So eventually you went to another slushy part of the country for graduate work? It snows in Boston, [Massachusetts], pretty regularly, I'm sure.

WATSON: [Yes]. Not as cold as Iowa.

GRAYSON: [. . .] So now you go to MIT and you've got to figure out somebody you want to work for.

WATSON: Well, again, I didn't very carefully research the faculty. [. . .] When I was applying to graduate school and when I went on my way to MIT, the only thing I knew about mass spectrometry was what I learned on that couple of pages in my physics book on electricity and magnetism where the magnetic sector mass spectrometer is an elegant example of the use of those phenomena.

I am embarrassed to say that I didn't know that Klaus Biemann was at MIT before I got there.[2] But upon interviewing the faculty it was clear that I wanted to work for Klaus Biemann on a project combining a gas chromatograph with a mass spectrometer through an interface that was all-glass so that sensitive molecules like alkaloids and steroids could be analyzed.[3]

GRAYSON: Before we go further there, I'd want to just check on one thing and that was what did it cost to go to Iowa State? Do you recall?

WATSON: A few hundred [dollars]. It was just amazing. I remember it was just a few hundred dollars for tuition and [. . . .] I lived in Friley Hall which was renowned as the largest dormitory under one roof on earth. [laughter]

GRAYSON: And so the expenses for room and board, and tuition were—

WATSON: In the order of hundreds.

GRAYSON: Manageable.

WATSON: Absolutely. I just don't understand why students these days are ostensibly racking up tens of thousands **<T: 30 min>** of dollars in loans. I was fortunate in that I had worked in the bluegrass harvest and had earned enough money to pay for my room and board and for my tuition. That and what my parents were willing to contribute. So I did not have to work during my undergraduate student days. I could focus solely on my studies. I was involved as I said before in the administration of a social fraternity, Theta Xi, which took a fair amount of time but

[2] Klaus Biemann, interview by Michael A. Grayson at Alton Bay, New Hampshire, 29 August 2006 (Philadelphia: Science History Institute, Oral History Transcript # 0279).
[3] J. Throck Watson and Klaus Biemann. "High-Resolution Mass Spectra of Compounds Emerging from a Gas Chromatograph." *Analytical Chemistry* 36, no. 6 (1964): 1135-1137.

was a rewarding experience in terms of taking care of a fairly large group of people and the fraternity house which was a fairly big enterprise in itself.

GRAYSON: So that was well within reason in terms of expense when compared to today's—

WATSON: Indeed, it's just extraordinary.

GRAYSON: Of course everything was cheaper then but still—

WATSON: [Yes], gasoline was twenty-five cents a gallon.

GRAYSON: [Yes], I remember that. All right, so we're back at MIT now. I just want to touch on that because it's interesting to keep tabs on what people have to toss up to the schools in that period compared to today. So you met up with Klaus Biemann who was . . . he had only been there probably less than a decade by then I would think?

WATSON: That's correct.

GRAYSON: But had established a reputation I believe by that time?

WATSON: Yes, He is an organic chemist by training, and was at MIT first as a postdoc and then when I got there he was a professor.

GRAYSON: Had he written the book by then?

WATSON: He had just finished writing his book [on] organic applications of mass spectrometry when I arrived.[4]

GRAYSON: And so he posed some possible research problems for you?

[4] Klaus Biemann. *Mass Spectrometry: Organic Chemical Applications* (New York: McGraw-Hill, 1962).

WATSON: Yes, he offered me the possibility of learning—or developing methodology—to sequence proteins by digesting them into peptides, making volatile derivatives of those peptides to be analyzed by mass spectrometry to learn their sequence. Overlapping sequences of the peptides would then spell out the sequence of the mother protein and I thought that . . . . I told him that I thought that was a little bit too much organic chemistry for me and I'm sure that offended him but being the gentleman that he is, he had another more mechanical project, that of using an effusion device somehow out of perforated or sintered glass to set up conditions of effusion to selectively remove the lightweight helium carrier gas coming from the gas chromatograph from the vaporized analyte having molecular weight to the order of two or three hundred. That turned out to be a very interesting challenge. He insisted that the device be made of glass. There could be no metal, there could be no microvalves, so all the rather easy connections that would **<T: 35 min>**be imagined were precluded in his requirement.

GRAYSON: And that was why?

WATSON: Because metal surfaces at two or three hundred degrees centigrade provides an active surface for decomposition of thermally sensitive labile materials, as were the alkaloids of interest to him steroids of interest to many people and so those were the criteria that I had to meet.

GRAYSON: And the idea of using the effusion, that was his idea?

WATSON: Klaus's idea was to establish effusion, and he suggested a very clever preliminary experiment to see if this was going to be at all feasible using pieces of classical glassware available to chemists; those including fritted or sintered glass components that are used in organic syntheses in many cases, or in filtering, or in isolating of certain chemicals in classical wet chemistry laboratory experiments. And once we proved the efficacy in establishing the conditions of effusion which was molecular flow—and that is to say the conditions for that are well-described in physics as being the discriminating interface had pores in the sintered glass, the diameter of which was about 0.1 the mean free path of the gaseous mixture and that would allow, in principle, for good separation based on inverse square root relationship of mass to effect the discrimination by preferentially thereby pulling off or pulling away the helium leaving behind the enriched analyte vapor to go into the mass spectrometer which had a fairly limited value of the pressure that could be tolerated in the ion source., Vacuum pumps at that stage were hard-pressed to keep up with the leaks in the gaskets to the flanges of the mass spectrometer. There was no way they could accommodate the flow coming out of [. . .] a packed column and so it was necessary to reduce the flow that would eventually go into the mass spectrometer, so that was the challenge.

GRAYSON: I know that Klaus had a time-of-flight instrument in his laboratory at one time that he used kind of like for proof of principle experiments. Is—

WATSON: [Yes]. So my prototype studies were carried out on the Bendix time-of-flight mass spectrometer, taking pictures of the mass spectra on the oscilloscope with a Polaroid film. [laughter]

GRAYSON: So you use these like sintered pieces of glass with effusive properties in time-of-flight to experiment with—

WATSON: [Yes], **<T: 40 min>** some Rube Goldberg experiments showed that, in fact, useful discrimination against the low molecular weight or low mass carrier gas could be achieved by establishing the conditions of effusion where the pore size was the order of microns. I don't remember exact dimensions but the order of microns.

GRAYSON: And then eventually you came up with this concept where there was a tube of effusive glass. That was—

WATSON: [Yes], so once we established the efficacy of the idea then I designed a more flow-friendly [design] where with great difficulty and bribes of a bottle or two of Jack Daniels we got the glass-blower to construct from fritted glass bubbling tubes that are used to degas solutions in organic chemistry or in any solutions; to physically drill [a] hole to make this pod of fritted glass into a tube—a fritted glass tube—that would be part of a continuum of capillary going into the fritted glass tube. And then the fritted glass tube had to be glass-blown to yet another capillary to make a final reduction in pressure going into the mass spectrometer. So this was a nightmare for the glass-blower, and I spent a lot of time cajoling him and finding out that Jack Daniels was one of his favorite beverages. Because under glass-blowing conditions the porous glass effectively exploded because the glass pores, of course, were filled with air and when that got heated they just exploded. But miraculously he was able to make one complete assembly, and I think we never got a second one. I remember I had a troop of my sibling graduate students [run interference for me at various intersections in the hallway] as I went down the hall from the glass blower carrying this delicate piece of glass. I couldn't afford to bump into someone coming around a blind corner and smashing this precious piece of glass. That was pretty good.

GRAYSON: So you actually had to take a piece of fritted glass that was designed for a completely different purpose and drill a hole through it and then have the glass blower—

WATSON: Then use that as a tube.

GRAYSON: To put together into the—

WATSON: To fuse to the end of that capillary which could be collapsed to a small orifice to establish the pressure drop necessary to achieve conditions of molecular flow in the fritted tube.

GRAYSON: [Yes]. So he was a pretty good glass blower?

WATSON: [Yes]. He wasn't all that patient but I spent a lot of time . . . we became friends. But, you know, buying a fifth of Jack Daniels on the graduate student's salary was a **<T: 45 min>** handicap.

GRAYSON: An investment.

WATSON: That was a big investment, but thank goodness he was able to make at least one work. I think we never got a second one.

GRAYSON: But then once that proof of principle had been demonstrated I think you could actually buy these tubes, fritted glass tubes, from Dow Corning [Corporation], or I know we could buy the subweights of an effusion separator.

WATSON: Where would you buy them?

GRAYSON: I don't remember but I know we bought some because then we did some experiments comparing the different types of molecular separator devices and I guess we bought it from Dow Corning, I don't know but I mean—

WATSON: I'll be darned.

GRAYSON: I think there's one . . . we might even have one at home. We got one of those deals. Or we gave it CHF [Chemical Heritage Foundation]. I don't know.

WATSON: I think there was something. Apparently, these were available on the RMU [Hitachi mass spectrometer model RMU-6] or something, Varian [Associates] or something. I can't remember.

GRAYSON: Well, the instrument manufacturers picked up on it quickly.

WATSON: [Professor O. David] Sparkman. Sparkman would remember these things.

GRAYSON: [Yes]. So that was basically your thesis topic?

WATSON: [Yes]. The dissertation topic was based on . . . . And we eventually used this separator after being optimized on the time-of-flight mass spectrometer. We adapted it to fit on the ion source of a double-focusing magnetic sector mass spectrometer where we used [a] photo plate to detect the [ions] . . . so you know which had the advantage of sort of a ray detection but also an integrating effect of the ion current that of course fluctuated in unison with the partial pressure of the analyte as it emerged from the gas chromatograph.

GRAYSON: So at this particular point in Biemann's career he had a probably pretty decent stable [group] of students.

WATSON: Yes.

GRAYSON: Who were your graduate siblings at the time? Do you recall?

WATSON: Well, my siblings included Dominic Desiderio and Paul Vouros, John Hayes, and, just as I was leaving, Ron Hites joined the group.

GRAYSON: What about Al [Alma] Burlingame? Was he a previous—

WATSON: [Yes], Al Burlingame was leaving about the time I was finishing my experimental

work. And Jim McCloskey was in residence for most of my time and was a valuable consultant to me on many things during graduate school, graduate life and . . . .[5]

GRAYSON: Well, that's a very interesting group of people for sure.

WATSON: Oh, it was wonderful. Then I had friends from other parts of chemistry, notably John Deutch who was in theoretical chemistry or quantum mechanics, and eventually we were roommates **<T: 50 min>** on Commonwealth Avenue in Boston and would have many good visits as we commuted across Harvard Bridge from Boston over to MIT, spending nights at the library waiting for the bus to take us back across Harvard Bridge at night. And, of course, John Deutch not only was interesting but, of note, he became eventually the director of the CIA [Central Intelligence Agency] in recent years.[6]

He had gained notoriety in Washington, DC, from early stages of our careers and graduate school together. Early he was chosen as one of Robert McNamara's "Whiz Kids" in the [Department of Defense] and so I think it's through those connections that John was tapped to be Director of the CIA.[7]

GRAYSON: How did he get noticed by McNamara?

WATSON: I think Deutch's father was an ambassador somehow or was somehow involved in government, so John became well-networked into the Washington hierarchy and society, so to speak, at an early age, and that eventually turned into summer jobs and I guess the Whiz Kids group was more than a summer job but he retained that.[8]

GRAYSON: But you say he was studying theoretical chemistry?

WATSON: Yes, he was in . . . well, quantum mechanics. What do you want to call that?

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[5] James A. McCloskey, Jr., interview by Michael A. Grayson at the McCloskeys' home, Helotes, Texas, 19-20 March 2012 (Philadelphia: Science History Institute, Oral History Transcript # 0702).

[6] John Deutch served as Deputy Secretary of Defense from 1994 to 1995 and as Director of the Central Intelligence Agency from 1995 to 1996.

[7] Smith, W. Thomas, and Thomas W. Smith. *Encyclopedia of the Central Intelligence Agency*. Infobase Publishing, 2003, 75.

[8] John Deutch's father, Michael J. Deutch, was the deputy director of the War Production Board during World War II and was part of a group that developed the method for making synthetic rubber out of petroleum. See "Michael Deutch, 88, Co-Inventor of Method for Synthetic Rubber," New York Times, last updated February 22, 1996, http://www.nytimes.com/1996/02/22/us/michael-deutch-88-co-inventor-of-method-for-synthetic-rubber html.

GRAYSON: [Yes], that's theoretical chemistry.

WATSON: [Yes]. And in deference to John I took a course in quantum mechanics with lectures from Paul Slater and I was totally lost. I never could catch on to the philosophy but interestingly enough, I was sitting in a lecture on quantum mechanics by Paul Slater the afternoon that John F. Kennedy was shot and Paul Slater walked in and announced that the president is dead. Wow. So we were stunned of course.

GRAYSON: [Yes].

WATSON: Still am. But I mean those guys think in integrals, differential [equations]. . . I just couldn't. I mean, I just knew shit from apple butter about what was going on. I talked to John about it a little bit but I didn't want to talk too much because I'm sure it just embarrassed the hell out of him that . . . how could he be talking to a turkey like me?

GRAYSON: So you had a fairly normal graduate experience, [. . .] four or five years with the Biemann lab?

WATSON: I think I was there exactly four years. Because it turns out that I had a commitment to go on active duty in the Air Force so I think I was on . . . . I had a delay from active duty to go to graduate school and I had to finish the graduate school at a certain time. I think that's what helped establish the short tenure, so to speak.

GRAYSON: Well, then we have to find out a little bit about your **<T: 55 min>** commitment. How did that come about?

WATSON: [. . .] So I went through the advanced ROTC [Reserve Officers' Training Corps] program at Iowa State University. At the end of which I was commissioned as a second lieutenant in the USAF [United States Air Force], and then I got a delay from active duty to go to graduate school and the delay from active duty had time limits. I had to finish the degree within a certain period of time.

GRAYSON: So there was a certain amount of, "Let's get it done and get out of here," kind of a thing?

WATSON: [Yes].

GRAYSON: And your decision to go into the military was for any particular reason?

WATSON: Well, yes. Well, I just felt an obligation. I had cousins that ran across Normandy Beach, [France], in 1944. I felt if they had to do that; I had to do something. So I just . . . I wasn't drafted, but I had to go into ROTC. It was part of the program at Iowa State. Everyone had to go into ROTC.

GRAYSON: For the first two years?

WATSON: For the first two years, but I just decided to apply for and was accepted into the advanced program and was being cultivated because I didn't wear glasses. Most of my classmates who were in the advanced program at Iowa State wore glasses and they, of course, did not qualify for flight training and so that was a path that they were hoping I would follow. And I did and I actually enjoyed summer camp very much and after exciting rides in jet aircraft including an F-100 and a refueling mission of a B-52 I was pretty excited about flying. And I almost committed myself but I was under the impression that it was going to be a three-year commitment but as it got down to the wire they said, "That's going to be five years." So that realization plus the realization that I was not a likely candidate to be a "top gun," I didn't figure I was that gung-ho on a daily basis. I was afraid that I'd probably push the wrong button someday in the cockpit and either go flying out through the canopy or somehow they'd be washing me off the runway with a hose, so I declined going into pilot training.

GRAYSON: But you did stay for the three-year—

WATSON: I did stay for the three-year commitment and I was eventually—well, as it turns out the Moffett Field [Moffett Federal Airfield] in Palo Alto, California, had a famous scientist who was studying chemical evolution. Cyril Ponnamperuma arranged for me to go work at Moffett Field as a civilian pending my orders to report for active duty. So in fact I worked at Moffett Field in the Ames Research Center with Cyril Ponnamperuma **<T: 60 min>** on chemical evolution which simulated primitive conditions on earth in ancient times where they were using electrical discharges in flasks containing nitrogen gas, water vapor, and—

GRAYSON: [. . .] Was he in the Air Force, Ponnamperuma?

WATSON: No, so it turns out he was at Ames Research Center, turned out to be at Moffett Field which was a navy base, and I was in the Air Force. And Ponnamperuma was trying to get me cleared to serve my military tour in his laboratory at Ames Research Center.

GRAYSON: Right. Here was a second lieutenant with a PhD in analytical chemistry.

WATSON: Yes.

GRAYSON: So it's, "Oh, these guys don't come along too often."

WATSON: [Yes]. So it finally came down to a discussion, between a general in the Air Force and an admiral in the Navy. And the general said, "We need Watson at the USAF School of Aerospace Medicine," where we were simulating conditions of the manned orbiting laboratory in a closed environment and they had a mass spectrometer, but they didn't have anyone that understood how to use it. Turned out to be a time-of-flight, by the way.

GRAYSON: And the admiral said?

WATSON: "No deal." Well, it was [what] the admiral wanted because that was the Navy base. And that's where . . . . I don't really understand the complexity but Ames Research Center, I guess, was part of the Navy base. So the Navy was going to have to get the Air Force to let me go and that didn't work out.

GRAYSON: So you never got to work with Ponnamperuma? Or you did?

WATSON: I did for a month. And we did some standard experiments of identifying from the brown gunk that formed in these spark chambers . . . I actually isolated amino acids. And it was amazing what they found in this gunk where this had high-voltage arcs simulating lightning in this primitive atmosphere of nitrogen.

GRAYSON: Of nitrogen?

WATSON: No oxygen. I guess maybe there was a limited amount of oxygen. I think the early atmosphere apparently was mostly reducing.

GRAYSON: [Yes]. So you only got to work for a month because the Air Force says, "You're going with us."

WATSON: "You've got to report to San Antonio, Texas."

GRAYSON: Okay. So now here you are a second lieutenant PhD, analytical chemist.

WATSON: At the School of Aerospace Medicine and they were, among other things, studying the stress of confinement on these pilots that had been talked into going into this altitude chamber. So that's where I got my interest in steroids and in biomedical applications of mass spectrometry which we didn't do much of there, but I saw the potential for that interaction and that helped me establish the focus of research in my **<T: 65 min>** early career, which eventually directed me to the Division of Clinical Pharmacology at Vanderbilt University where I worked with prostaglandins.

GRAYSON: So what did you do besides this experiment with Aerospace Medicine? You were there for what? Was it all three years, that whole time you were there in San Antonio?

WATSON: [Yes].

GRAYSON: This was at about the time Vietnam was heating up, wasn't it?

WATSON: [Yes].

GRAYSON: And then nobody came around and said, "Hey dude."

WATSON: [Yes]. That was always a possibility. I mean, I was not looked at from a distance as a mass spec guy. I was looked at from a distance as a chemist, and they could just as well have said, "We need a chemist to check the pH in these deltas." You know, that was always a possibility, but I never saw action in the Vietnam combat.

GRAYSON: There was never any effort to move you away from this job at aerospace medicine into a bit more military role?

WATSON: No.

GRAYSON: I mean, that worked out for you because I think Vietnam left a bad mark on a lot of people that went there.

WATSON: Yes, indeed. Yes, and I felt like I should go. I mean, you know, with your guys dying over there why should I be sitting around my Boy Scout camp over there at Brooks Air Force Base, but that's what I did because that's what my boss told me to do. And I was shielded in a way.

GRAYSON: [Yes]. So was there any mass spec involved in that Brooks Air Force Base, at—

WATSON: [Yes]. A principal concern for the manned or rigged laboratory were what kind of materials would accumulate in the atmosphere of the closed environment? And so that was our mission. As it turned out it there were pretty good scrubbers to pull things out of the closed atmosphere and so there never seemed to be any threat of poisoning due to any organics building up other than what was coming out of the fabrics of the materials in the . . . . And so, as it turned out, mass spectrometry—we didn't do anything significant.

In fact, what I did was help develop methodology to determine plasma levels of testosterone because there was concern [. . .] about the impact of confinement on endocrinology and so we were gearing up. And in fact I developed methodology based on mainly gas chromatography, but as backed up GC-MS [gas chromatography-mass spectrometry] for plasma testosterone because many of my colleagues at the School of Aerospace Medicine were new MDs who had been drafted, effectively, to serve a tour of duty at the School of Aerospace Medicine <**T: 70 min**> to participate in these experiments where individuals would go into altitude chambers for weeks, if not months, at a time, and in an environment of 30 percent oxygen as diluted by helium at a total pressure of a third of an atmosphere, which turns out to be the pressure at ten thousand feet. But more importantly that was the pressure that could be held or confined or . . . [yes], pressure that could be held in a spacecraft that was . . . well, there was a limitation. I mean, the Russians had powerful enough rockets that they could blast off spacecraft that could withstand one atmosphere of pressure differential and they had a shirt-sleeve environment: 80 percent nitrogen, 20 percent oxygen.

The US had to have a lighter payload which meant that the spacecraft was not as strong as the Russians which meant that the total pressure differential could be no more than a third of an atmosphere.

GRAYSON: That was the environment that they had to establish for these guinea pigs?

WATSON: [Yes].

GRAYSON: Now I understand one time they thought of using, instead of a mixture of oxygen and helium, they thought of using pure oxygen.

WATSON: Yes. In fact that was the protocol for the beginning of the space program. Apparently all of the space shots, perhaps even including John Glenn, was that he was in 100 percent oxygen.

GRAYSON: At a reduced pressure but still 100 percent oxygen?

WATSON: [Yes]. And this was all because of payload. They couldn't . . . well, they had to have 100 percent oxygen so that you get enough on each breath and at 30 percent oxygen in helium at one-third of an atmosphere there was enough oxygen pulled into the lung per breath that led to a partial pressure of oxygen in the blood stream that is the same as that achieved in the normal atmosphere of only 20 percent oxygen because it was enriched.

GRAYSON: But using 100 percent oxygen even at reduced pressure was dangerous.

WATSON: It was certainly dangerous. It was an unbelievable fire hazard and some **<T: 75 min>** colleagues died in a fire in our building due to an electrical spark that ignited clothing in 100 percent oxygen and it was about that time, within weeks or months, that the astronauts, three astronauts burned to death in the space capsule on top of the rocket when there was a fire in the spacecraft at 100 percent oxygen so it's a very dangerous situation.[9]

GRAYSON: And when that they gave up using?

WATSON: I'm sure that's true.

[9] On January 27, 1967, a fire occurred in the pure oxygen environment in the Apollo 1 command module before launch. The fire killed all three astronauts on board. See "Apollo 1: The Fire," NASA, accessed on April 16, 2015, http://history nasa.gov/SP-4029/Apollo_01a_Summary htm.

GRAYSON: [Yes], well, it's too dangerous.

WATSON: [Yes].

GRAYSON: So we had three years of kind of . . . what would you call it? Human endurance research in the Air Force looking at the . . . and then looking also at whatever compounds might accumulate that—

WATSON: [Yes], sort of an environmental control. And assisting with stress on the endocrine system due to confinement and any aberrations in atmospheric conditions. You know, it wasn't expected that helium would have any effect, but it was necessary to have the experiment to prove that it had no effect and it did not.

GRAYSON: [Yes], very good. Now your three-year hitch is coming up to an end. So you're having to think about your future from here. You're done with the Air Force, you've satisfied your obligation. Where do you go from there?

WATSON: [Yes]. I continued to realize my deficiency in organic chemistry and so I had met through James McCloskey, who was then at the Institute for Lipid Research at Baylor Medical School [Baylor College of Medicine], that he had a visiting scientist from France in his lab whose name was Robert [E.] Wolff—

GRAYSON: Very French-sounding.

WATSON: And Robert Wolff was an organic synthetic chemist—organic synthesis chemist, I guess I should say—and Robert Wolff was interested in my coming to his lab as a postdoc to help his efforts to develop GC-MS on a French mass spectrometer and he would also provide, for my benefit, a research project that would involve my learning organic synthesis techniques to install deuterium atoms at specific sites in long-chain organic acids.[10] So this was an opportunity for me to learn practical organic mass spectrometry on the job, so to speak.

GRAYSON: In organic synthesis?

[10] Robert E. Wolff, J. Throck Watson, and Brian J. Sweetman. "Utility of dicyanomethylene derivatives in structural studies of long-chain aliphatic acids by mass spectrometry." *Tetrahedron Letters* 11, no. 31 (1970): 2719-2722.

WATSON: In organic synthesis. And it was a very interesting project and it provided me with organic chemistry skills **<T: 80 min>** in a practical sense that became quite useful to my early career research at Michigan State in the laboratory manufacturing, among other things, diesel methane, a dangerous but convenient means for producing methyl esters of fatty acids which was of interest to me. [. . .]

And so that I became a postdoc which would turn out to be very useful and very enjoyable. It was at Strasbourg, [France]. [. . .] Institut de Chimie, Université de Strasbourg.

GRAYSON: Ah, so how is your French? I mean, you're going to France. Can you speak French?

WATSON: Ah, un peu. Je peux parler quelque mots. Mais c'est ne pas grande chose.

GRAYSON: Okay.

WATSON: Je peux commander le viand et le vin dans le restaurant.

GRAYSON: All right, I don't speak French, so we're in trouble. But it was an experience, I'm sure.

WATSON: Oh, it was wonderful. Strasbourg is such a wonderful [. . .] little city. It's a wonderful place to have lunch. So I spent a year there.

GRAYSON: Besides having lunch what did you do? Scientifically, what did you do there? You were learning some organic chemistry?

WATSON: Well, interestingly enough Robert Wolff had the idea . . . . Somehow he had found out that making a dicyano derivative of . . . imagine a carbonyl in a carboxylic acid group and somewhere he read that a dicyano derivative had the same electronic structure as a methyl ester of same carboxylic acid. So he thought it might behave similarly under fragmentation conditions, EI [election ionization], but it didn't. It formed an unbelievable picket fence of peaks, which I told Mike Gross was [a] perfect example of remote site cleavage. [laughter]

I showed him that on a **<T: 85 min>** site visit once when he was site visiting me. I don't think he was impressed. But in order to try to figure out the fragmentation mechanism, I

synthesized these deuterium-labeled analogs of the carboxylic acid and then made the dicyano derivative thereof, and that was Robert Wolff's interest. And it was an interesting thing, but I learned all these techniques in the process of making these analogs. And that's pretty neat, to make an analog where there's two deuterium atoms on the alpha carbon and another where there's hydrogen [atoms] on the alpha carbon and deuterium is on the beta carbon and so that was . . . I learned a hell of a lot.

GRAYSON: Well, you had a year there, right, to learn all that good stuff?

WATSON: [Yes], but I was not the best set of hands he ever had and he let me know that. He was not a very tactful person.

GRAYSON: But it was good for you to get that experience.

WATSON: Absolutely. It served me very well.

GRAYSON: So what else? Was there anything interesting going on in France while you were there that kind of gives us a sense of the time? This was what, the late sixties?

WATSON: Well, it was when . . . the manned landing on the moon. [Neil Armstrong]. Where he's, "One giant step for mankind and . . ." or whatever in the Sam Hill that was . . . .

GRAYSON: I guess that was covered pretty intensely in the French [media].

WATSON: Yes, oh yes.

GRAYSON: The Americans were good guys then, huh?

WATSON: Yes.

GRAYSON: We're still good guys.

WATSON: [Yes], and they were pleased to see the success of the launch and the landing.

Wow, it was a big deal. I felt like a hot shit. Like, "I'm an American!" And I remember other postdocs, one guy from Britain [United Kingdom] was really disdainful of [US] involvement in Vietnam, and I always said, "Well, shit, we've got treaties. What if we had a treaty with Great Britain and you guys got attacked by Germany? You want us to come to your rescue?" [laughter] You know, so we did have that con game in South Vietnam.

GRAYSON: [Yes].

WATSON: It turned out they were frauds, I guess. I never did figure out what happened. Did you?

GRAYSON: Well, I think what happened was the mentality of the time was that it was a domino effect. You know if you let Vietnam go to the Communists, South Vietnam go to the Communists then this would go Communist and that would go Communist, and the Communists would end up taking over that part of the world. We'd all be in deep doo-doo if it breaks here to the Communists, so there's no question about that, and I think that's probably what drove us more than anything is this fear. [. . .]

[END OF AUDIO, FILE 1.1]

GRAYSON: [Yes], well, where were we? We were talking about your extended tour in France where you learned how to do organic synthesis and you labeled compounds as deuterium and that was after you finished a three-year stint in the Air Force. [. . .] You were talking about France and the attitude of the French towards Americans at that time. It was fairly favorable. And so are there interesting things that you had to observe about France at that particular time that you want to share with us or is that about it?

WATSON: Well, that was my postdoc time. Well, the interesting thing is what little French I know I learned by going to lunch with the graduate students and eating in their cafeteria which was pretty interesting. You know they have an established meal, and you just go along and get a dollop of this and a dollop of that and by and large it's pretty good and you go and you sit down and the cafeteria on more or less picnic benches and there's carafes of wine brought to the table. White or red or both.

GRAYSON: So wine is a—

WATSON: A staple.

GRAYSON: You drink in the day with a soda and water or whatever?

WATSON: [Yes], I think there was also water available. I think so. Anyway.

GRAYSON: Not everybody had wine, though.

WATSON: Well, I don't think there was any abuse.

GRAYSON: Well, it was lunch and you had to go back to the lab.

WATSON: [Yes], well, that's a good point. But anyway wine is pretty well where the meal is. It's not like Dick Cheney having only one beer before he goes out and shoots his buddy in the face.[11] [laughter]

GRAYSON: Okay. As a hunter I assume this probably resonates with you even more.

WATSON: [Yes]!

GRAYSON: By the way before breakfast we were talking about when you were an undergraduate, you took a summer job abroad.

WATSON: Oh, in Bavaria, [Germany].

GRAYSON: [Yes]. Can you tell us about that? [. . .]

WATSON: Well, let's see. When I was at Iowa State, I was in a fraternity and one of my

[11] In 2006, Vice President Dick Cheney accidentally shot his hunting companion, Harry Whittington, while quail-hunting on a Texas ranch. Mr. Cheney described having had beer at lunch, several hours before the hunting excursion. See "Cheney: 'One of the worst days of my life," CNN.com, 16 February 2006. http://www.cnn.com/2006/POLITICS/02/15/cheney/index.html?PHPSESSID=16f421bb29284bc67718636a74d7656b

fraternity brothers had joined an organization called American Student Information Service which was a euphemism for a commercial equivalent of a student exchange program except that it was commercialized to the extent that you had to buy a membership, and if you bought a membership this organization would try to find you employment somewhere in Europe for the summer. And my fraternity brother wanted me to do that, and I told him I couldn't because I had an obligation to work with my father during a summer harvesting bluegrass. And so my fraternity brother went ahead and joined the organization, and had lined up a fairly cushy job at a resort somewhere on the Rhine [River] and continued to badger me and chide me a little bit **<T: 05 min>** for passing up the opportunity to spend time with him on the Rhine.

And meanwhile, my father finally told me that we weren't going to do any bluegrass harvest that summer and so I was suddenly free to do whatever I wanted for the summer. So I went back to my fraternity brother and we decided that I would write a letter to the American Student Information Service saying that I wanted to join the organization provided that I was assigned to the same job that my fraternity brother had.

GRAYSON: You wanted to stick together and be pals?

WATSON: [Yes], I wanted to continue having my buddy with me so to speak. So, fine, I sent the letter off and about six, seven weeks later we each get a letter from the American Student Information Service saying that he and I were assigned to farm labor in Southern Bavaria.

GRAYSON: That sounds like an exciting activity.

WATSON: [Yes]. So my fraternity brother was not particularly excited about that but accepted it and so we flew . . . at that time we flew turbo prop airplanes from La Guardia [Airport], stopped in Reykjavik, Iceland to refuel for a couple of hours, and we met other people on the airplane that were going over to Europe and they were also ones that had arranged for a job in a resort and were, sort of, chuckling at us who were assigned to farm labor, for crying out loud, like we were convicts!

So we landed over in Frankfort, [Germany], and got on a train, went down to Munich, [Germany], took another train to a small city in Bavaria called Traunstein, [Germany]. [. . .] Our destination, however, was a village called Waging am See, [Germany]. And a middle-age man met us at the train center there in Waging who turned out to be the straw boss on the farm where we were going to work and he took us to a tavern, promptly ordered a couple of steins of beer and a couple of glasses of whiskey for a boilermaker or whatever. That was our introduction. Then he drove us out to the farmstead and we went to bed for the night. I remember that the windows in the bedroom opened out with no screens, no windows, just shutters that opened out into the night. We were effectively in the foothills of the Bavarian Alps.

This farm was owned by an elderly gentleman who lived on the place. They had not only a barn but a fairly big house for the main family **<T: 10 min>** with the old man and his wife. They had two daughters in their twenties or thirties and one was married to the guy who picked us up at the train. [He] turned out to be our straw boss, and also of note this guy had been a captain in the German Army in the artillery under General [Erwin] Rommel.

GRAYSON: So he was stationed evidently in North Africa?

WATSON: Africa probably. And it turned out he was a very nice guy, and he loved Americans and I'm not sure whether he had spent some time in an American POW [prisoner of war camp] but, anyway, he had a good attitude toward us.

GRAYSON: The father—you said one of them had a kind of a Nazi . . .

WATSON: So the old man had . . . I don't know how to describe it, but (a) he, sort of, looked like a Nazi, and (b) he had, sort of, a stern look about him and attitude. And he walked around the farm as we were working and making sure we were . . . . He had a walking stick, and he had riding pants for horseback, and he wore a leather or a herringbone tweed sports coat and a typical German hat that you would see from Bavaria with feathers in it and so forth.

So the family in this house consisted of the old man and his wife. It was an older lady and their two daughters and one of the daughters was married to the captain under Rommel, and he was our straw boss, and the young wife could speak a little bit of English like, "open the window, close the door," sort of thing and we spoke hardly any German. I mean, "Ich spreche kein Deutsche." I mean, it was silly thing to say but we tried to learn various phrases and various words every day and we got along just fine.

We worked hard. We worked ten hours a day, five days a week. On Saturday we could take a bath and on Sunday the artillery captain and his wife and the two kids would take us on a Sunday drive. We'd drive up into the mountains—the Bavarian Alps—and go to various activities in the village. So we were part of the family. It was wonderful. My fraternity brother and I did lots of odd jobs, mostly things that no one else wanted to do like clean the manure out of the barn and just odd jobs around the place that needed to be done, we would do them.

GRAYSON: But you ended up working basically pretty long days?

WATSON: [Yes], so we'd work ten hour days. Among other things this farm was a mixed bag of growing crops like wheat, hay, possibly corn. But they also had a truck garden and among other things, sugar beets; and we had to go out and hoe the sugar beets, weed the sugar beets and

I remember that we had quite a bit of rain and it was a lot of mud out there. So we were more or less hoeing the sugar beets in the mud. It was a mess, but **<T: 15 min>** we didn't complain too much because everyone else was working hard, even the straw boss. And you couldn't complain too much in that beautiful country but all you had to do was just look up from where you were hoeing the sugar beets, look across the valley at the Bavarian Alps, snow-covered.

It was *Sound of Music* country; it was just gorgeous. [. . .] We'd get up and have breakfast in the morning, go down to the main table in the dining room and the table had various loaves of bread, big plates of butter, bowls of jam and that was breakfast, and you could have coffee. No bacon and eggs, just bread and butter, and sweet jam and stuff.

I had trouble eating enough of that to keep me going until noon but about eleven o'clock we would come back into the house for lunch, and it wasn't lunch. It was a huge meal. At each of the place settings there would be a bowl of hot soup and then there would be big plates of meat, like a big beef roast or a pot roast or a pork roast and big bowls of potatoes and big bowls of gravy and vegetables of some sort, I suppose, I can't remember what, but it was a big, heavy meal and about one o'clock we'd go back to work, back out in the field, no dessert, back in the field. And we'd work for a couple of hours and then about three o'clock we'd go back to the house and the table was set with huge plates of cookies or cake or pie or strawberry shortcake, just wonderful desserts and that would be middle of the afternoon and then we'd work until seven o'clock at night, and then we'd go back to the house, wash up, go back into the big table with the whole family and at each place setting was a bowl of soup but it was cold soup and then we'd bring out big trays of sandwiches. It'd be two slices of bread and butter or two slices of bread and cheese, or two slices of bread and salami or something like that. But it was a cold meal, cold sandwiches as opposed to the huge dinner that we had for lunch, quite different. And then we'd go to bed about seven o'clock, 7:30, something like that. We were pretty tired, I'll tell you.

First day, they got us up at seven o'clock after getting there the night before and having the beer and the whiskey with the straw boss. First day we were out putting up green hay which in this country we called silage. It was green hay that would be sent or windrowed into a shredder of sorts that would chop this green hay up and it would be put in some sort of silage to be fermented to be fed to the cattle during the autumn and winter, I guess. That was tough work because it was all intertwined and like a mess of twine that had been tangled. It was not hay that was nice, fluffy and dry, that you could move around easily. It wasn't baled. It was just a mess.

GRAYSON: So how long is this tour of duty? [. . .]

WATSON: We worked there for three or four months as I recall. Then I had a cousin who was on duty in the Army, stationed in Germany, and he came by and offered to take us on a little tour of Europe, much to the chagrin of the old man and the straw boss who were depending on us to work in the harvest. And so we did as much as we could with them but they sympathized with us and let us go. [laughter]

GRAYSON: Well, it was nice of your cousin.

WATSON: It was a wonderful, wonderful experience living with this family and living in that small village, and in contrast when we returned to the United States, of course, we went back to Stuttgart, [Germany], or wherever, or Frankfurt—I can't remember where—got back on the plane and met many of the same students that we had visited with on the way over from Iceland and they were still kidding us about having to work on a farm and everything but we asked them what they had done.

Well, they had worked in resorts all summer, waiting on tables filled with Americans. It was like they had been working in St. Louis, [Missouri], at some bar. They had never set foot in a domestic household in Germany, had no contact with the German population and, in contrast, we had had this wonderful experience with a family, and we kept in touch with that family for many months. A wonderful experience.

GRAYSON: Yes, all because of your fraternity brother.

WATSON: [Yes]. He got over it. Oh, mercy!

GRAYSON: So then we can kind of fast-forward back out to when you had finished off your postdoctoral tour in France. So you had a little bit of European experience there going to both Germany and France. I mean it was kind of really interesting and fun.

WATSON: [Yes]. And that tour around with my cousin. I remembered never having had a bad meal in France. So I took the opportunity to go back to France at my first opportunity which happened to be that postdoctoral experience at Strasbourg.

GRAYSON: So he took you around not just Germany but other places in Europe besides Germany?

WATSON: [Yes]. But we visited, among other things, Neuschwanstein [Castle], this wonderful castle.

GRAYSON: That's an amazing place.

WATSON: Oh, [yes]. We went to Italy. We traveled. We went to Pompeii, Naples, Rome. Oh, it was wonderful.

GRAYSON: So you were wrapping up your postdoctoral stint. Now you've got to find someplace to work. And you're pretty much committed to academia by now. You're not interested in going into industrial facilities?

WATSON: I think that's right. I had my sights set on some academic job, if I could find one, and as it turned out my good friend, James McCloskey had apparently interacted with—perhaps on a site visit—some faculty at Vanderbilt University in pharmacology and he knew that they were starting a division of clinical pharmacology where they were going to use a mass spectrometer to help with the methodology and they were looking for a person that might help them set that kind of analytical facility up. **<T: 25 min>** I applied for that and went back to the United States and went to Vanderbilt, gave a seminar and ended up being hired upon return from Europe which was the start of my academic career. Suddenly I was Assistant Professor of Pharmacology.

GRAYSON: [Yes], I was wondering about how you got into the pharmacology business.

WATSON: And at that point I didn't know the difference between pharmacology and pharmacy. I sat in on the course—the main course—for pharmacology first year and got myself oriented.

GRAYSON: So what is the difference between them?

WATSON: Pharmacy is the formulation of drugs for ingestion. Pharmacology is a study of the mechanism of action of the drug.

GRAYSON: So it's like pharmacy research, you'd say?

WATSON: Well . . . and clinical pharmacology in particular was directed toward drug interactions but, of course, all that required a knowledge of the mechanism of action of the drugs of interest. And usually the interactions could be explained by the commonalities of the mechanism of action, but I was working with John [A.] Oates who was the Division Chief of Clinical Pharmacology at Vanderbilt. He was starting a program where he wanted to get into the prostaglandin field, and so I helped set up methodology that would be able to detect and

quantitate endogenous prostaglandins using stable isotope-labeled analogs as internal standards. A methodology not totally unique to what we were doing there at Vanderbilt because investigators at the Karolinska Institute in Stockholm, [Sweden], were already doing that kind of approach, but they needed to have that kind of methodology set up at Vanderbilt to support the clinical pharmacology studies of . . . with the putative involvement of prostaglandins.

GRAYSON: So why the interest in prostaglandins?

WATSON: Well, it was a new and coming field . . . . It was about this time that John [R.] Vane from Great Britain had discovered the mechanism of action of aspirin, namely that it is an inhibitor of cyclooxygenase, the main enzyme in the biosynthetic pathway of prostaglandins from the precursor of arachidonic acid.[12] And so there were many ancillary therapies ongoing at Vanderbilt that required knowledge of whether the cyclooxygenase pathway was extant, and so the **<T: 30 min>** analytical methodology based on mass spectrometry for prostaglandins and thromboxanes was of paramount importance to the clinical pharmacology group at Vanderbilt.

GRAYSON: Thromboxane? That's another class of—

WATSON: That's an alternate pathway to prostaglandins. Also coming out of all of these are in the so-called arachidonic acid cascade. Prostaglandins and thromboxanes are downstream metabolites of arachidonic acid.

GRAYSON: So you're really into . . . kind of biology, biochemistry as well as when you get to this pharmacology business.

WATSON: [Yes]. Well, pharmacology is a fascinating field. You know, if I had it to do over, I might well go into pharmacology. Pharmacology is a wonderful mixture of biochemistry, physiology, analytical chemistry, anatomy. It's very interesting.

GRAYSON: [. . .] So it was basically your skillset in mass spectrometry that—

WATSON: Oh, that made me [attractive]. Absolutely.

[12] Salvador Moncada, Sergio H. Ferreira, and John R. Vane. "Inhibition of prostaglandin biosynthesis as the mechanism of analgesia of aspirin-like drugs in the dog knee joint." *European journal of pharmacology* 31, no. 2 (1975): 250-260. Vane would win the Nobel prize for this work in 1982.

GRAYSON: What kind of equipment did they have?

WATSON: So they had an LKB [LKB Instruments]. [An] LKB-9000 had shown up on the loading dock at Vanderbilt Medical School, and they didn't know what to do with it. So they were delighted that I showed up. [. . .] So I opened the box, took out the LKB and set it up, got it running. Today the platform on which the LKB was mounted for shipment from Stockholm resides in my workshop in the barn as a work table. So the LKB-9000 is a magnetic sector mass spectrometer, single-stage, single-focusing.

GRAYSON: Was getting it functional a problem? Was it very—

WATSON: No.

GRAYSON: Straightforward?

WATSON: Pretty straightforward.

GRAYSON: The biggest problem was you had a difference in power requirements. So did they already include a transformer for that?

WATSON: Someone took care of that. It ran on 220 [volts], I'm pretty sure. I mean, most everything in Europe is 220 still. It was probably an issue with a phase, but I didn't have to figure that out. There were electrical people that got that squared away under the auspices of LKB installation engineers.

GRAYSON: So they did send an engineer to help install?

WATSON: [No]. They did not. I mean, LKB had centers of technical support in the States, I think on the East Coast, probably in the Washington DC area as I recall, Maryland . . . .

GRAYSON: So they gave you phone support or gave Vanderbilt the phone support how to . . . what to do?

WATSON: Well, just to get it installed. And then I took over as far as getting it running and showing its relevance for prostaglandins and establishing detection limits, linearity of calibration curves, etc., etc., etc.

GRAYSON: Did it have the jet separator on it?

WATSON: [Yes]. It had the stainless steel jet separator which is a diffusion-oriented separator, **<T: 35 min>** as opposed to the effusion-based separator and molecular flow that I developed at MIT. So it worked just fine. I didn't have a problem with that. This was designed by Ragnar Ryhage at the Karolinska [Institute]. [. . .] [Yes], so I was the mass spec guy.

GRAYSON: Now did you have any students there, grad students?

WATSON: I had one and I wanted to . . . but you know I was in pharmacology.

GRAYSON: So you were not in a traditional chemistry setting?

WATSON: Absolutely not.

GRAYSON: Or analytical chemistry?

WATSON: I was in a traditional pharmacology setting. And the graduate students wanted to work with someone who was doing blood and guts experiments. You know, like you walk down the hall in a pharmacology department and every other lab you see a dog laying there, disemboweled and catheters and all kinds of things through its heart and through its lungs and through its liver, and doing metabolic studies and, you know, all kinds of blood and guts type stuff, like that. And I wasn't doing anything like that. And so my students, so to speak, were postdocs who were coming to learn clinical pharmacology, and they would work with me to learn methodology that would be important to their current project and to their future career elsewhere in clinical pharmacology; and so I had to set them up with selected ion monitoring for their particular molecule, and it wasn't always prostaglandins.

It could be other drugs because there were a lot of hypertensive studies going on in clinical pharmacology and these people had clinical appointments. Most of my colleagues, MDs my age, were heavily into hypertension. Usually figuring out protocols for monitoring or figuring out drug interaction problems.

GRAYSON: So when you're using the term "clinical" I get the sense that it has a very specific meaning.

WATSON: Well, what that means is that your experimental animals are human beings. [laughter] That's the key issue. That's what distinguishes pharmacology per se and clinical pharmacology is that the experiments **<T: 45 min>** are done on humans with consent, but they are very heavily, very, very super heavily monitored. So it's good if you want to get close medical attention as a patient in a hypertensive test, man, you get very careful scrutiny.

GRAYSON: They'll keep a close eye on you?

WATSON: [Yes].

GRAYSON: Now did you actually . . . were you in a position to teach any classes?

WATSON: Well, the pharmacology course at Vanderbilt was team-taught. We'd all give two or three lectures, so there was very little teaching. In my case I was given the topics that nobody else wanted to lecture on.

GRAYSON: Because you were the outsider?

WATSON: I was the new boy. So I lectured on antihistamines. I lectured on anti-malarials, and I lectured on prostaglandins because there was no expert on prostaglandins. So I had to learn about that which was not too tough. There wasn't much known about it.

GRAYSON: So basically this was explaining the action of these various compounds?

WATSON: No. What?

GRAYSON: Your lectures on the antihistamines and anti-malarials and the prostaglandins.

WATSON: Those are just topics that I had to research and come up with a lecture.

GRAYSON: Ah, okay.

WATSON: On anti-malarials, there was a presumption of expertise or knowledge of parasitology of which I had zero. I spent a hell of a lot of time just trying to get myself up to speed with where the medical students were, because this was given [. . .]

So the pharmacology course was the course offered by the pharmacology faculty to the medical school class. So we would go in as teams. The next few lectures are going to be on pharmacology and here are the topics and here are the guys who are going to give the lectures. The teaching load was very light in pharmacology. People had clinical responsibilities elsewhere, except for me, but I was on the list of instructors going in front of one hundred ten medical students.

GRAYSON: [Yes]. I was asking about how big those classes are.

WATSON: You know, it was one of the top medical schools in the country, and here I am giving lectures to them. Are you kidding? I'm just a pharmacologist. Are you kidding me? [laughter] Oh, shit! Oh, mercy!

GRAYSON: Well, apparently you succeeded.

WATSON: Well, you know I've got to brag a little bit. I think it might have been after my lecture on antihistamines that the class stood up and applauded. And I had seen that with none of the other faculty. So, you know, I was scared into really researching it, you know, and studying like crazy to give these lectures because, this is all new material to me. So it was just that I had given apparently a very systematic lecture that they could tune into.

GRAYSON: Well, apparently you're communicating material which is **<T: 50 min>** what they . . .

WATSON: [Yes]. So that was quite rewarding.

GRAYSON: Now did you do this like for the whole time that you were at Vanderbilt, this team teaching this stuff?

WATSON: [Yes].

GRAYSON: So this is part of your career there?

WATSON: [Yes]. I was on the faculty. I was a faculty member at pharmacology which was a joke, but when I would zoom in on an area I would do the best I could. And I think my knack for … my book's success… is that all my writing was done in the context of remembering how I encountered those topics. I mean, there were books when I was a graduate student early on with the words on the front cover, "Introduction to Mass Spectrometry," and I would read those books and I couldn't understand what the hell was going on. So when I wrote my book I had "Introduction to Mass Spectrometry" as a title but I wrote it based on how I remember encountering the topic and had that, kind of, empathy so to speak for the reader.[13] And I think that's what made my book popular enough to ask for another edition. [. . .]

When I started to write the book, I remember my boss, John Oates, when I started to write the book was a little reluctant to have me do it because he knew what I was getting into and I didn't. But he said, "You know, Jack. . ." And he was talking from the standpoint of his physician students. "They don't need to know the alignment of the slits and they want to know what the impact is on . . . what do you need? What kind of sample do you need? What do the data look like?" And he said, "Why don't you come up with half a dozen simple, simple, simple examples where you show what certain things mean?" And so I came up with this nice—I still love it—this example of the mass spectrum of acetone, showing a molecular ion, how it fragments in a decomposition manner based on odd electron movement, that **<T: 55 min>** explains homiletic cleavage and eventually heteroletic cleavage, and the difference between the mass spectrum . . . .

So I chose the example of acetone and acetaldehyde. Those are isomers. They have the same molecular weight. So if you were only to do the mass you wouldn't know which one you had but if you let it fragment they fragment differently, vastly differently to give a characteristic and interpretable mass spectrum. And that didactic example was in my first edition and it's in the fourth edition.

GRAYSON: So you decided to do this book project while you were at Vanderbilt?

WATSON: [Yes]. Well, what happened was that before I left Europe I went up at the request of Vanderbilt . . . because I had already gotten the offer from Vanderbilt and they said go up and visit Bo [R.] Holmstedt at the Karolinska. He was a fairly well-known—internationally known

[13] J. Throck Watson, *Introduction to Mass Spectrometry: Biomedical, Environmental and Forensic Applications* (New York: Raven Press, 1976).

actually—psychopharmacologist. And a publisher called Raven Press had contacted Bo and asked him to write a book on mass spectrometry and Bo says, "Shit, I don't have time for that." And I had just visited his lab and I guess he took a liking to me, and so he told Raven Press to contact me at Vanderbilt and so I was gullible enough to . . . . You know, it was publish or perish. Here's an opportunity to write a book, for Christ's sake. [laughter] I didn't know. Oh, my gosh. What a nightmare! How many books have you written?

GRAYSON: Well, the only thing I've ever gotten involved in is editing *Measuring Mass,* so I never wrote a book. I was an editor.[14]

WATSON: [Yes], it's just an unbelievable exercise in organization and tough work research-wise. [. . .]

GRAYSON: Okay, we'll take a break here. [recording paused]

It's recording. So [yes], Bo Holmstedt. [. . .] You went to the Karolinska Institute before you left France.

WATSON: Before I left Europe.

GRAYSON: Before you left Europe for Vanderbilt?

WATSON: [Yes]. The Vanderbilt people, faculty, the chairman and the new director of the clinical pharmacology division at Vanderbilt knew that Bo Holmstedt was at the Karolinska and that he had an LKB and that it wouldn't hurt anything if I went up there and just visited with him. And so I did. And, furthermore, I wanted to go to Copenhagen, [Denmark], and have some beer and so forth and it was a nice little visit. And as it turned out, as a result of that, Bo got me this recommendation which got me into the book-writing business. [. . .]

GRAYSON: For which you're ever-thankful, right?

WATSON: Oh, [yes]. Well, it was such a nightmare, you know, just keeping track of the figures because in those days that was when we still . . . having a figure was a matter of a drawing **<T: 60 min>** that was done with block print somehow by a draftsman and then they'd

[14] Michael A. Grayson. *Measuring Mass: From Positive Rays to Protons* (Philadelphia, PA: Chemical Heritage Foundation, 2002).

take a photograph of the darn thing. And so I was coming up with all of these figures, and figure seventeen might be three by four feet in dimension, and figure twenty-seven might be the size of a 3 × 5 card, and just keeping track of where those were, and then writing about them and then having a photograph taken which would then be submitted with a manuscript was a real headache. And then there was, of course, the task of writing something; you know, the agony of the first draft—oh, the agony!—and I was just overwhelmed trying to keep track of all that.

GRAYSON: Well, at least you didn't have that many classes to teach.

WATSON: [Yes]. My teaching load was not at issue. That was right. It was just the book, but it was just the management of my own activities relating to the book. It was a massive project, and I would write it out long-hand on paper and give it to the secretary who would give me a draft, and then I would have to correct the draft, of course, then she'd make typos in the second draft. And there was no word processing; that is to say you couldn't go back and correct a line.

But I remember when [. . .] IBM came out with, sort of, a word processor, something that would at least allow you to repeat a paragraph somewhere that you could actually correct so that when it printed out the hard copy would show the edits. It was a big deal. So in contrast with that, this last—our fourth edition [with David O. Sparkman]—I typed virtually every word on my laptop and did my own editing.

GRAYSON: That was in two thousand and—

WATSON: I started that in 2002.

GRAYSON: Okay. And we finished in 2007. And then David Sparkman and I would fight and argue over the first draft [of the fourth edition] which was, of course, of prime importance. We finally had a foothold and then we'd fight and scream over various presentations, various descriptions, but we're still good friends. But all those arguments I'm sure made it a better book because it was really the reader was the beneficiary, as it should be.

GRAYSON: I mean, you had two knowledgeable people debating the issue of how best to present the topic.

WATSON: That's right.

GRAYSON: And if you're working with someone who's knowledgeable then that's okay, but

you sometimes get stuck with someone who's not knowledgeable and so that's a little bit different project. So you started the first book [first edition of *Introduction to Mass Spectrometry*]. Was it shortly after you got to Vanderbilt?

WATSON: No. It was well into it. I was . . .

GRAYSON: You waited a while. Did this mean—

WATSON: Well, this all happened, you know. I didn't initiate anything. Raven Press contacted me and I gather, I mean, I could figure it out **<T: 65 min>** time-wise, but it was five or six months after I got to Vanderbilt.

GRAYSON: And so you acquiesced and you say Oates was a little bit . . . was trying to save you from yourself here?

WATSON: Well, I think he knew that it was going to take a lot of time and that was going to take away from my duties as the mass spec expert serving his research program. But on the other hand, I think he also realized that it was going to be a feather in the cap of not only me but of his faculty and his research and his . . . . And we had a center grant from NIH [National Institutes of Health], a center for clinical pharmacology, and there were many, many, many different facets of which analytical chemistry was an important one, and mass spectrometry was an important sub-facet of that.

So he saw it as somewhat of a dilution of my efforts in his interest area maybe, but he also saw it as an asset for renewal of the grants that supported the whole thing. Showing that on [an] international level we had expertise in certain areas. So I did it. Oh man, what a job. I mean I finally got down to the point when our children were young, and they were at this stage waking up at six o'clock in the morning and sometimes even before that. [. . .] And so I would get up with the kids and go down to the basement where I had an old door set up on saw horses to serve as a huge desk to keep track of all these aspects that I was working on. Where was figure thirty-seven? Where is reference sixteen and who is the third author on reference twelve, and all that which is so easy to figure out these days with computers but at that time I was using a pad of paper and a pencil and a ballpoint [pen] in writing long-hand and in keeping track of this stuff by making notes to myself. [. . .] It was exhausting, and it seemed hopeless. I couldn't see the end. [. . .] I was in quicksand. It was frightening.

GRAYSON: So how well was it accepted when it got published?

WATSON: It was accepted. I mean, my colleagues even said it was remarkable, and I couldn't believe they were saying this

GRAYSON: So it was well worth it?

WATSON: Well, I guess. I mean, what makes it worth it is when someone comes and tells you that it helped them. And this really hit home to me one time when I went to the ASMS [American Society of Mass Spectrometry] meeting. At the ASMS meeting **<T: 70 min>** when you register you go to the registration desk and that's often manned by a graduate student from some laboratory other than your own. [. . .] At one time I went to the registration desk and the young man says, "What's your name?" And I said, "Watson, Jack Throck Watson." And he says, "Oh, I read your book and it helped me so much!" I mean, this is an unsolicited testimonial . . . that means the world. This makes suddenly all this agony of writing the damn thing worthwhile. [. . .] And the students that I had at Michigan State in the chemistry department who were taking mass spectrometry from a collage of different mass spectrometry books; the word got around that the one to read first was mine and they told me so and that meant a lot to me. That meant an awful lot to me. The few thousand dollars I've made from royalties, it's just utterly ridiculous what that amounts to in terms of pay per hour. I stopped making the calculation because it's so pathetic and depressing.

GRAYSON: So you started out there assistant professor, so you were granted tenure in '73 [and heard about it] at ASMS?

WATSON: At Vanderbilt, [yes]. I was made an associate professor with tenure.

GRAYSON: [Yes]. So that was a nice step forward.

WATSON: [Yes]. And then [Charles C.] Sweeley called me up one day and said he was stepping down from director of the mass spec facility at Michigan State and wanted me to interview for the position. I said, "Chuck, you're [of] too big a stature for me to come up there and do that." He says, "I'm done." Well, good old Chuck. I've known him for years.

GRAYSON: So he actually invited you to apply for the position?

WATSON: [Yes], he was lock-stepped with me every step of the way, making sure that I got in the door.

GRAYSON: So this is towards the end of his career?

WATSON: [Yes]. So the deal was that there was a need for a new chairman of biochemistry and he wanted that. So he was [. . .] wanting to unload the mass spec facility responsibility which was that of being the principal investigator of an NIH research resource . . . oh, why do I have to tell you? [laughter]

GRAYSON: [Yes]. I know how NIH uses resources, [yes].

WATSON: [Yes], and he was tired of all the administrative bullshit that goes along with that and Klaus [Biemann] had warned me about that. Klaus hated all the administrative bullshit. But, you know, you've got to take some bullshit to get the jewels.

GRAYSON: So those grants usually run, like, five years, right?

WATSON: [Yes].

GRAYSON: And so **<T: 75 min>** how long had the grant been there?

WATSON: It was . . .

GRAYSON: When you came, I mean, usually they're, you know . . .

WATSON: [Yes]. He initiated it and I think it was established in 1968.[15]

GRAYSON: That long?

WATSON: I think. You know, I've got the data somewhere, but is that important?

[15] Sweeley joined the biochemistry department at Michigan State and established the mass spectrometry project there in 1968. See Charles C. Sweeney. "Reflections on my career in analytical chemistry and biochemistry." *Proceedings of the Japan Academy, Series B Physical and Biological Sciences* vol. 86 no. 8 (2010): 822-836. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3037520/

GRAYSON: No, it's just the idea that it was a fairly well-established operation at the time.

WATSON: Absolutely.

GRAYSON: And he had invited you to come on board and I guess he wanted to keep that facility there.

WATSON: That's right, he did.

GRAYSON: Because you know it had a certain amount of panache to it to have that recognition from the school.

WATSON: So he had been through two renewals, I think.

GRAYSON: Okay. So that would have been like the late sixties. [. . .]

WATSON: It was late seventies—are you putting those dates in there?

GRAYSON: [. . .] Just an approximate date is fine. The whole idea that it was an ongoing concern that it was set up and functioning—

WATSON: That's right. So . . .

GRAYSON: They wanted someone to carry it on or to continue it.

WATSON: [Yes].

[. . .]

GRAYSON: Now you're in more of a natural setting, you might say, in the chemistry department?

WATSON: [Yes]. So part of my agreement to come to Michigan State was that I get an appointment in chemistry.

GRAYSON: You didn't want this pharmacology stuff?

WATSON: [Yes]. Being at Vanderbilt in the medical school is like being in the Air Force and not being a pilot is the way I felt about it. I was just not one of the boys. And I tried to get an appointment in chemistry. Basically, the answer was that [yes], I was a nice guy and everything but they didn't say it exactly but in essence I was going to be a **<T: 80 min>** threat to depleting their pool of graduate students. I probably would have pulled several.

GRAYSON: So even though you approached the chemistry department at Vanderbilt they were—

WATSON: They did not entertain that.

[. . .]

GRAYSON: But that was a condition that you made going to Michigan State is that you wanted to be a member of the chemistry faculty.

WATSON: Correct. [. . .] My primary appointment was in biochemistry. My secondary appointment was in chemistry. [. . .]

GRAYSON: [. . .] Now you [were] able to accept graduate students [. . .] when you moved to Michigan State?

WATSON: [Yes]. I had a lot of graduate students. **<T: 85 min>** [. . .]

GRAYSON: So this was obviously it was a major step up in your career.

WATSON: Absolutely, it was a quantum step.

GRAYSON: Were most of these people coming to you with an interest in mass spectrometry?

WATSON: [Yes].

GRAYSON: So you gave a spiel [to] entering graduate students and they got the message that was something they wanted to get involved in.

WATSON: [Yes]. I gave them the point that I was biomedically oriented and it was mass spectrometry working with biomolecules. And that sounded attractive to a lot of them plus it was well-known that I had a lot of money. Because I took training as a very serious issue in my RR [Research and Related] budget. I really pumped it in there [. . .]

GRAYSON: So basically you managed the resource all the way up through 1999.

WATSON: I suppose.

GRAYSON: Is it [the mass spec center] still at Michigan State?

WATSON: No. We lost [it] in ’99.

[. . .]

GRAYSON: After you had been at Michigan State for a while you had this sabbatical leave to Paris, [France], a school—École Normale Supérieure, Lab de Chimie with Christian Rolando. That sounds like fun. **<T: 95 min>** When was that? I mean, what did you do there?

WATSON: Christian Rolando is a remarkable guy. He is a fantastic combination of organic synthesis chemist, computer expert, both hardware and software.

GRAYSON: So how did you—

WATSON: At ease and enjoys tearing equipment apart and rebuilding it or—

GRAYSON: Modifying it.

WATSON: Yes, and he's a fun guy, and he has wild and interesting ideas. He's just really great. But when it came time for me to go on sabbatical I asked the [Riber-Nermag] near mag people where I could . . . . I wanted to go to Paris. I wanted to do a sabbatical in France and I said, "Who would be good to work for?" And they said, "Christian Rolando." Well, it turned out they were right. Christian Rolando was just bringing to operation a pentaquadrupole: five quadrupoles. What this means is that you can manufacture by ion molecule collisions, reagent ions to send into a reaction chamber to undergo reactions and use the fifth quadrupole to analyze the products thereof. Pretty clever, eh?

GRAYSON: Now these quadrupoles are not aligned in a linear fashion?

WATSON: Yes.

GRAYSON: They are? One after the other.

WATSON: [Yes]. It's sort of like a triple-quad except it's a penta-quad. And he built it. He's a little like me in that he never . . . I mean, he never throws anything away. In this case it's the radio from the Riber quadrupole back in 1950 but, you know, there will be a use for it. [. . .] He would do hydrogen discharges to make a high concentration of hydrogen atoms which, of course, are very reactive. But he had this wild discharge.

GRAYSON: I mean, that's going back to the beginning.

WATSON: Sort of violent, and he'd have that be right on the source and he had no fear. [laughter] Anyway that's how it came about that I went to École Normale Supérieure, which is the Harvard [University] of France.

GRAYSON: And so using this penta quadrupole to—

WATSON: We did some wild-ass experiments. Some of my grad students had started with

[Christie Enke] and did it better with Christian Rolando because we could control the reagents. [. . .]

GRAYSON: Must have been a fun year.

WATSON: It was great fun. Plus, I got to eat in a French restaurant every night. [laughter]

GRAYSON: And by 1988 I guess the French attitude towards Americans had mellowed some. But it's still pretty appreciative.

WATSON: I think it was. **<T: 100 min>** I never had any problem. I don't know which trip it was but when I was in southern France one time, somehow I got in a conversation where I could, sort of, understand what they were saying, but some of these old Frenchman had heard that I was an American and they were saying thank you to me for 1944.[16] I said, "Don't thank me; thank my cousins." It was my cousins who ran across Omaha Beach. They went in on the seventeenth run, so it wasn't hell as it was in *Saving Private Ryan,* which you probably saw. I mean, can you imagine the horror of that? I can't.

GRAYSON: No.

WATSON: But my cousins didn't have to tolerate that. They probably got some flak but when they got to the top of the ridge they had to go through the hedgerows where the Germans were entrenched and they slept in the mud for months. One of my cousins was one of the first guys across the Rhine in the Battle of the Bulge and his platoon was decimated. As they crossed the Rhine the Germans let them get about 80 percent of the way across and they opened up on them.

GRAYSON: Wow.

WATSON: It took all night, he said, for some of these guys to die. [. . .] He never recovered—post-traumatic stress syndrome. [Yes], he was a casualty mentally.

GRAYSON: So what do you think were your most important developments for science when you were at Michigan State?

[16] The Allied liberation of France during World War II began in 1944 and continued into 1945.

WATSON: My graduate students. And of course, all these students that I had from chemistry, I had to come up with an analytical project, a project that would meet the demands of the analytical chemistry group and also satisfied the needs for these students to get a flavor of biochemistry. So one of my postdocs pointed out to me we were . . . all of a sudden in the beginning of the FAB [fast atom bombardment] days. I just had a new postdoc come in who had been studying x-ray crystallography of proteins at Purdue [University] and he wanted to get some experience in mass spectrometry. He turned out to be the resident expert in proteins. Not by mass spectrometer. None of us knew what the hell to do.

It was John [T.] Stults who began to get us into the peptide sequencing business in a serious manner. It turned out this guy from Purdue [Eugene Zaluzec] had a lot of experience with sulfur chemistry. And at the FAB time [. . .] some of our service clients were interested in cysteine, the amino acid that forms disulfide bonds. And it became as simple as are there any cysteines in my peptide and, if so, how many?

And, of course, that was when we didn't have very good accuracy on our FAB and so there was a lot of error in the determination of the M or Z value of the protonated molecule. And so our idea was to make a derivative of the cysteine by adding something to it that would greatly magnify its mass. Among other things you could add a mercury atom or you could add some other chemical that would make a covalent bond with the cysteine and you knew what you were doing chemistry-wise and so you knew what the mass of the additive was and that then told you . . . it made it easier to . . . you got a higher mass and exaggerated at the site of cysteine. So we were sort of getting in the business but then postdoc Eugene pointed out to me one day some work that had been reported by chemists [Abraham Patchornik and Y. Degani] at UCLA [University of California, Los Angeles]. What those guys did was make a thiocyano group added to the cysteine.

Well, that was no big deal, really, but what was interesting was that when they took this thiocyano derivative of the cysteine peptide and put it in a solution with a nucleophile like ammonia it caused a rearrangement of that moiety resulting in cleavage of the peptide bond, cleavage of the peptide chain on the amino terminal side of the cysteine. So that was just another chemical tool we used but I finally realized that, you know, it wasn't just that we were adding a certain mass. It was that we had available to us a pair of chemical scissors that we characterized and could trust to cut at a certain place, and we knew what it did. It made an amino thiazolidine **<T: 110 min>** and we knew what the mass of the amino thiazolidine was and we knew what the sequence of the protein was and so . . . if you don't know how many cysteines there are you could pretty easily figure it out from what I've already told you.

But once you figure it out that's the easy part. If it's oxidized, the difficult part is determining which cysteine is hooked to which cysteine. I realized on the way to a reverse site visit in Washington, DC that different pairs of cysteines form a disulfide bond when subjected to the chemistry that I have told you about cyanylation and cleavage would give a different set of cleavage products that would unambiguously identify which cysteines were connected to one

another.[17] I thought it was going to be fabulous and at that time I had an absolute genius chemistry graduate student, [Jiang Wu], who could actually speak English and he was a computer nut. It was a great story.

GRAYSON: So what's a reverse site visit? I mean, you've got site visits. I understand that but a reverse site visit is . . .

WATSON: Is when you go to Washington and the study section meeting takes place there.

GRAYSON: Ah, okay.

WATSON: So it was one of those situations where we had gotten a bad score and we were—I don't know what the . . . it was not a renewal but a second chance sort of thing, a revised application sort of thing.

GRAYSON: I guess the old slap on the wrist, something kind of deal, got that kind of penalty.

WATSON: It was definitely . . . well, it was better than never getting funded again. And, in fact, I think this cyanylation idea really sold them. They really loved it. So, I should tell you about this. I was having trouble getting funded by writing R01s and having them be reviewed by mass spec-oriented study sections because it became pretty clear to me that the mass spec people did not understand the problem of disulfide bond structure. So I complained to the secretary and he said, "Fine, so you don't like mass spec people who you think don't understand the project; send it to me again, I'll see that it gets to a study section heavily populated by protein chemists." And we did and he sent it to [them] for review. They loved it, and I got very high marks and I was delighted, of course. I had a new postdoc come in. He [Brett Phinney] fit right in perfectly. We were off roaring. We even got into protein folding using the same cyanylation methodology as a sideline, and I brought in a protein folding guy [Chad Borges] who had some publications. I had six or seven publications which I thought was pretty decent.[18]

And so I put in my final review, my final grant application. I said, "I need [to] renew." So I decided to go ahead and write up the renewal and send it back to this study section that was so enthralled. And I thought we had a great chance of being funded, and I said to myself, "If I get funded, fine, I'll hang on. If we don't get funded, to hell with it, I'll go fishing."

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[17] Jiang Wu and J. Throck Watson. "A novel methodology for assignment of disulfide bond pairings in proteins." *Protein Science* 6, no. 2 (1997): 391-398.

[18] J. Throck Watson, Y. Yang, and J. Wu. "Capture and identification of folding intermediates of cystinyl proteins by cyanylation and mass spectrometry." *Journal of Molecular Graphics and Modelling* 19, no. 1 (2001): 119-128.

Well, it got trashed. It got triaged. This study section that had been so excited had suddenly been repopulated with x-ray crystallographers. They said, "This is not a mass spectrometry problem. This does not require mass spectrometry. X-ray crystallography can handle this." And those x-ray crystallography people . . . . I mean, I have followed their work carefully. They do so much by analogy or by similarity. They'll say, "Well, the x-ray data will show that this group is analogous to that group and therefore the disulfide bond has to be this way," and there's no direct proof. It's all by analogy—no hard proof—and they lynched me and I just said, "To hell with it, I'm going fishing!" So that was the end of that show.

GRAYSON: Well, you can beat your head against a brick wall only so long.

WATSON: But I was so happy to find a study section that appreciated what I was doing from an area that I really was an expert in, namely proteins. And the mass spectrometry was trivial. There was nothing imaginative from the mass spectrometric point of view, which is why the study sections that were mass spec-oriented kept turning me down because it was just a molecular weight determination. It was nothing. **<T: 120 min>** Nothing to it, even though the outcome was—

GRAYSON: You were determining something valuable.

WATSON: Yes, but the mass spec people never appreciated that. [. . .] But the group had . . . on their reverse site visit I remember the review came back saying that we looked pretty good, and they alluded to what I just told you and they worded it like this, "Using a clever chemical approach, they've shown a way to elucidate disulfide bond structure." That was wonderful and this . . . it required a lot of wet chemistry and the wet chemistry required . . . it was difficult to get the stoichiometry right of the reducing agent because I had to reduce the existing disulfide bonds to get the mono or the . . . I forgot the word I used. [. . .]

GRAYSON: So you were talking earlier about something about hydrogen atoms and—

WATSON: What Rolando was doing?

GRAYSON: No. You wanted to talk about the fact that there's a difference between a hydrogen ion and a hydrogen . . . what was that subtlety? I didn't get the—

WATSON: Okay, do you do any teaching?

GRAYSON: No.

WATSON: Have you ever taught freshman chemistry?

GRAYSON: No.

WATSON: You ever teach acid-based chemistry to anybody?

GRAYSON: No.

WATSON: The simple little equilibrium that you write down: HA is the weak acid and that goes in equilibrium with an H^+, hydrogen ion and the conjugate base which is the A^-. Well, that H^+, is that a proton or is that a hydrogen ion or is it the same thing?

GRAYSON: It's the same thing.

WATSON: You mean, it's like in sodium there are thirteen protons and fifteen neutrons in the nucleus. Is one of those fifteen protons in the sodium nucleus the same as the H^+ in the equilibrium with the weak acid?

GRAYSON: No, it's the same as a proton and the hydrogen atom.

WATSON: [Yes], and that's not the H^+. So why do they call this H^+ a proton? They'll do that, right? That's what protonates the damn protein.

GRAYSON: [Yes].

WATSON: For MALDI. So where does that proton come from? Does it come from the nucleus of some atom?

GRAYSON: It comes from the hydrogen atom, doesn't it? If you take an electron away from a hydrogen atom you're going to get a protonated hydrogen atom . . . .

WATSON: Say that again?

GRAYSON: You take an electron away from a hydrogen atom, you're going to have a proton, a hydrogen nucleus.

WATSON: So is that what an acid does when it dissociates?

GRAYSON: Who knows? [laughter]

WATSON: See, I think we get carried away with our symbolism.

GRAYSON: Well, it's quite clearly a possibility. **<T: 125 min>**

WATSON: I, sort of, like the ionization business, the equilibrium, but you know the way we talk about it, it could just as well be a proton coming out of the nucleus of any atom as a proton. But it makes a wonderful little story, equilibria-wise to call it H^+. And in the acid-based chemistry associated therewith.

GRAYSON: So this sounds like a philosophical question.

WATSON: I think you're right. I think you're right. It's not—

GRAYSON: It's almost like the particle-wave duality.

WATSON: It's [. . .] semantics and philosophy and the duality of light.

GRAYSON: [Yes]. Well, I mean, science used to be called natural philosophy, right? [. . .]

WATSON: If I knew that I had forgotten it, but that's—

GRAYSON: Well, these guys you know from the early—

WATSON: Absolutely, you know, like Plato and those guys?

GRAYSON: Well, I'm going to [the] 1700s, even then, you know, in [Isaac] Newton's time, he was considered to be principally a natural philosopher. I think all these guys that looked at nature to try and understand it from a rational perspective, what we would call science today I think they thought of it more as natural philosophy.

WATSON: I see.

GRAYSON: But I'm putting words in someone else's mouth. [laughter]

WATSON: Anyway I think you're tuning into—

GRAYSON: What they call *naturlich wissenschaftler*, right, that's your German scientist?

WATSON: I guess.

GRAYSON: *Naturlich wissenschaftler*, nature, knowledge, art . . . the art of the nature of knowledge, and the art of the knowledge of nature.

WATSON: Wow. Well, should we go out and explore the country a little bit?

GRAYSON: [Yes], let's take a little break and go out in the woods. [. . .]

[END OF AUDIO, FILE 1.2]

GRAYSON: So one of the things that occurred to me is you started out at Vanderbilt with an LKB-9000. I would assume during your tenure there you purchased other equipment?

WATSON: Yes, we got a Riber-Nermag quadrupole.

GRAYSON: Any particular reason why you chose that instrument?

WATSON: Well, we had done some tests that gave the best results of reproducibility and detection limits of those that we tested at that time. As I recall that was the reason. And Sparkman was also around and encouraging as to go that direction, and it did have good resolving power where those big, long rods, according to Sparkman, was the reason, but we were just interested in reproducibility and detection limits and that was satisfactory.

GRAYSON: That was [a French machine]?

WATSON: Yes.

GRAYSON: [. . .] Did it perform up to your expectations?

WATSON: Yes, it was quite good.

GRAYSON: So were the specifications for resolving power and mass range pretty much standard for quads at that time?

WATSON: I'd say so, [yes].

GRAYSON: What's that got, like mass [five hundred] then—

WATSON: Or maybe more I think.

GRAYSON: And was that put in a GC [gas chromatography] method prior?

WATSON: Yes, GC mass.

GRAYSON: And did you have to introduce that yourself or did they provide—

WATSON: I think they must have done that.

GRAYSON: Provided some MS interface. Any other instruments while at Vanderbilt?

WATSON: No.

GRAYSON: And so was the LKB still functioning when you left there?

WATSON: Yes.

GRAYSON: Well, you know when you take good care of an instrument it should last for quite some time. And you had a pretty good stable of equipment at Michigan State, I would assume.

WATSON: [Yes].

GRAYSON: Do you recall when you started and then after Sweeley . . . was it Sweeley who got you there?

WATSON: [Yes].

GRAYSON: I guess they had an LKB-9000 there too, didn't they, when you came originally?

WATSON: Yes, they did.

GRAYSON: Because I thought that was one of the instruments that . . . and I've got a picture I think Sweeley and Ryhage in front of an LKB-9000. I think Ryhage came over or was in the States at one time or another for some event or whatnot and decided to visit Chuck in . . . . Any other instruments that you recall at the time?

WATSON: Oh, we had a . . .

GRAYSON: Probably some GC-MS.

WATSON: We had a JEOL HX-110, which is double-focusing, a very good instrument and also a JEOL-505 for GC-MS, also performing very nicely. You know the LKB and the 505 were used for metabolic profiling that Chuck had developed.

GRAYSON: He was a biochemist, wasn't he, or biologist?

WATSON: Biochemist, [yes]. His interest was in carbohydrates **<T: 05 min>** and lipids I guess I should say too.

GRAYSON: [Yes]. It's unfortunate that [we didn't have the opportunity to interview him.] . . . he's the kind of person it would have been interesting to talk to. And do you recall any stories that you told about his career or any things that would be kind of interesting for people today to know about Chuck Sweeley?

WATSON: Well, of course he was the guy that promoted the use . . . or actually illustrated or demonstrated the utility of trimethylsilyl derivatives of hydroxylated compounds, and he also pioneered the use of stable isotope labeled analogs of what he was studying as the internal standards.[19] Some, I think, he even used to determine the level of glucose in some of his initial experiments. But his main theme while at Michigan State was developing this technology of so-called metabolic profiling which was based on complete scanning of the mass spectrum and then at designated retention indexes, going into that database and searching for identifying ions, peaks that represented what I think he called marker ions.[20] And then he had confirming ions and then constructed an algorithm that pulled quantitative data out of these responses, so it was both qualitative and quantitative. And he was very heavily sought after for detection of and identification of metabolic defects. [. . .] Enzyme deficiencies that would lead to accumulation of some certain metabolites that would render clinical symptoms.

[19] C.C. Sweeley, Ronald Bentley, M. Makita, and W. W. Wells. "Gas-liquid chromatography of trimethylsilyl derivatives of sugars and related substances." *Journal of the American Chemical Society* 85, no. 16 (1963): 2497-2507.

[20] Stephen C. Gates, and Charles C. Sweeley. "Quantitative metabolic profiling based on gas chromatography." *Clinical chemistry* 24, no. 10 (1978): 1663-1673.

GRAYSON: When he got you to take over [the mass spec facility], he headed for the chair of the biochemistry department?

WATSON: That's correct, yes.

GRAYSON: A lot of people see the chairman position as a pain in the can.

WATSON: I sure would.

GRAYSON: He sought it.

WATSON: That's true, he did, and he did a good job. He was a great chairman.

GRAYSON: So basically you were in his department?

WATSON: That's right. He was also very careful because he was easily criticized for giving favoritism to [the] mass spec facility. He was actually hard on us. [laughter] But he gave important support when needed both at site visits; he was worth his weight in gold at site visits. He put on quite a show.

GRAYSON: And how big was the department that he was running? I mean, the mass spec facility was just part of this.

WATSON: The biochemistry faculty numbered [on] the order of forty faculty, including those who had appointments in other departments as well, but it's a big operation, and biochemistry was and still is one of the best departments on campus in terms of productivity and publications and so forth. **<T: 10 min>**

GRAYSON: And so he maintained that position for probably . . . into the nineties or—

WATSON: Yes.

GRAYSON: Before he retired from running the show?

WATSON: Yes. I don't know exactly when. I can't remember the date that he retired.[21]

GRAYSON: I remember they did this multiple ion monitoring activity.

WATSON: That's right.

GRAYSON: That was something that came out of Michigan State, wasn't it?

WATSON: Well, to some extent. He actually did that in Stockholm with Ryhage. He called it alternating acceleration voltage, AVA. [. . .] That allowed him to do multiple ion monitoring, but his big thing was this metabolic profiling which was based on complete scan processing, arrays of complete mass spectra.[22]

GRAYSON: Kind of like a preview of what's going on nowadays with them.

WATSON: Metabolomics?

GRAYSON: [Yes]. It's kind of precursor to metabolomics.

WATSON: [Yes]. Today's metabolomics is heavily dependent upon data processing.

GRAYSON: Well, the problem today is there's so much data processed and produced that who knows if anybody ever really understands everything or anything. And a lot of times people end up publishing stuff that has a rough time with reviewers. Did you have any particularly interesting or unhappy experiences when you were trying to get something that you think is valuable out and the reviewer just pans it because he misses the point?

WATSON: No.

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[21] Dr. Sweeley retired to professor emeritus in 1992.

[22] Charles C. Sweeley, William H.. Elliott, Ian Fries, and Ragnar Ryhage. "Mass spectrometric determination of unresolved components in gas chromatographic effluents." *Analytical chemistry* 38, no. 11 (1966): 1549-1553.

GRAYSON: That happens to some people but—

WATSON: Well, you mean me as an author?

GRAYSON: [Yes], you as an author writing scientific papers.

WATSON: No, I fared well with that.

GRAYSON: That's good.

WATSON: [. . .] I got as many critiques as I could before I let anything out. Locally. Even including grants. I didn't want to hear how good something was until after I mailed it off and before that I wanted as much criticism as possible. So that I could deal with it before it got in some remote smoky room behind closed doors where you can't defend yourself.

GRAYSON: You wouldn't have somebody come out of the woodwork on something that you, like you say, couldn't defend because you hadn't thought about or hadn't seen it that way. So do you think there are any particularly upsetting or bad events you might say in your career that had an effect on your career or just everything was hunky-dory?

WATSON: Ha!

GRAYSON: I mean, there's a lot of work but that's not a bad event. That's part of the game. [. . .]

WATSON: That's right. No, I had a good run.

GRAYSON: Well, particularly after you got to Michigan State when you can get graduate students . . .

WATSON: [Yes], well, I had a good number. I could show you downstairs the plaque. I had some forty or so graduate students, and it was a real beehive in the facility.

GRAYSON: So how many did you like to have at a time? Obviously, there's a balancing act between the two.

WATSON: Absolutely.

GRAYSON: So, I mean, do you have like three or six or—

WATSON: I like somewhere between six and twelve.

GRAYSON: That's a fairly large number **<T: 15 min>**

WATSON: [Yes], but it's good to have a large enough group so that the oldsters can teach the youngsters the ropes of the laboratory and that keeps the momentum.

GRAYSON: I know it seems more common nowadays to have undergraduate research being conducted. Did you have any undergraduates?

WATSON: Oh yes.

GRAYSON: Really? Okay. Did they find the experience sufficiently exciting to go on in science or to go on to graduate work?

WATSON: Well, especially there was a young man, Curtis Pickering, who was from the Flint, [Michigan], area and he was outstanding. He learned how to run the GC-MS instruments and the MS-MS [tandem mass spectrometry] quickly and participated almost immediately as a TA] for an ACS [American Chemical Society] short course, and he went on to a PhD program at UCSF [University of California, San Francisco] in biochemistry.

GRAYSON: That would be with Burlingame there then at UCSF?

WATSON: [Yes], but Burlingame had nothing to do with the project he was working on. I

think [it's] even a molecular biology type project he's working on, I have forgotten the details.[23] But he was highly-motivated and a very capable undergrad, left in good shape, and I'm confident he'll do well in both making contributions and being successful.

GRAYSON: So with forty graduate students you had to develop some mentoring skills, shall we say. Is there any particular . . . I mean obviously you're also kind of a bit of a psychologist. People come in with totally different ideas of what constitutes work—

WATSON: That's a good point. [laughter]

GRAYSON: And what constitutes getting the job done. So how did you develop . . . what was your mentoring style? I mean, some people just throw them in a *gemisch* and say, "Survive," which is a style but . . . .

WATSON: I usually would start a new grad student out as an assistant to a senior graduate student to help out with some of the mundane experiments as a means of learning the technology. And I put a high priority on group meetings, which we had every Friday afternoon, and I made sure that they were very informal and people could discuss things openly and take advantage of all the other brains in the room in terms of critique. After a given student would make a presentation of the work that they'd done since the last group meeting, then we'd have a question session. Everyone would ask a question. They'd go around the room and also going around the room the other graduate students would be asked to make suggestions on how to maybe pursue an alternate approach to the problem and so forth. So it was a learning experience for everybody and also it took advantage of the sum of the **<T: 20 min>** analytical minds that were there. I think it made the group strong. There was a lot of [the] buddy system going on.

GRAYSON: You must have had some postdocs in the lab, I would imagine.

WATSON: Yes.

GRAYSON: So they probably also helped out in the mentoring business, I guess, as you say.

WATSON: Well, the postdocs would also attend the group meetings, of course, and there were some projects where postdocs, as well as a grad student, would work on the same project to

[23] Curtis Reid Pickering. "Understanding the Early Events in Breast Carcinogenesis by Inactivating P16INK4a in Primary Human Mammary Epithelial Cells" (PhD dissertation, University of California San Francisco, 2008), http://gradworks.umi.com/33/24/3324574.html.

some extent or facets thereof. And then you're right. I mean, in many cases the ideal postdoc could very well be a replacement for me in certain cases especially if I were going out of town to a study section meeting or on sabbatical even. So there was good continuity that way.

GRAYSON: [Yes], and these postdocs would come in for, what, a one- or two-year appointment and move on?

WATSON: A minimum of two years.

GRAYSON: Minimum of two years. It's hard to do much in a year.

WATSON: And so postdocs might be there three, four years.

GRAYSON: And this was funding that you had to get though. You had to provide the funding for these guys, right?

WATSON: Yes.

GRAYSON: So that was a requirement.

WATSON: [Yes], well, and early on that came through the training part of the resource but later on it was simply part of my R01s, which was a great relief to write the R01 grants as opposed to the telephone book-sized grant applications for the research resource, which was just a sometimes unmanageable amount of administrative detail.

GRAYSON: [Yes]. I often wondered if anybody ever read those things besides the people who prepared them. So your funding came primarily from the research grant and some R01 grants?

WATSON: Yes.

GRAYSON: And those are mostly all NIH, I assume?

WATSON: Yes.

GRAYSON: Okay. You didn't try it for DOD [Department of Defense] or NIH?

WATSON: You mean NSF [National Science Foundation]?

GRAYSON: NSF.

WATSON: No.

GRAYSON: Now your resource had a lot of training but also did you run samples for outside schools—

WATSON: Oh, yes. [. . .] We had a service program.

GRAYSON: I always thought that was an important part of the activity although I think some of the resources treat that as a not-to-be-bothered-with very much activity.

WATSON: [Yes]. The manager of the facility was to interface with the users, and we had on-campus users and off-campus users and the service manager was heavily, heavily involved with the off-campus researchers both in planning the experiment so that the samples would be prepared properly for analysis and in the data analysis.

GRAYSON: [Yes]. I see also the opportunity to train students on different equipment and I remember in our group a student would be on a project in which he used one piece of equipment extensively and it was through the service project that he got to use the other instruments in the lab [. . .] because maybe the sample of it being submitted wasn't amenable to the instrumentation that he was most familiar with and so a lot of these new guys didn't particularly care to get service samples where we had to use the old magnetic sector dog **<T: 25 min>** but they learned.

WATSON: But one thing, to that point . . . participation in the ACS short course—the laboratory short course sections—where I asked or required the grad students to be teaching assistants in that context. That gave them opportunity to use a wider variety of instruments and techniques than they would otherwise have had exposure to in the context of their dissertation research.

GRAYSON: Sure.

WATSON: So it was a good symbiotic relationship.

GRAYSON: Well, I think it is important that these people come away learning or knowing more about other mass spectrometers than the one that they just did their research with or used in their research. [. . .] Did you get any financial support for the operation of your research from Michigan State or was it all off money or . . . ?

WATSON: We got some local money through a fee-for-service type arrangement with on-campus, non-NIH users.

GRAYSON: But the school per se didn't—

WATSON: Not when I was in charge. They finally have committed substantial continuing support for the mass spec facility as being a campus-wide analytical facility. There is a line item for that these days. But during my tenure it was quite variable.

GRAYSON: [Yes], well, money is . . . there's always money to be had in different places and getting it is always challenging. I was curious how you spent some time . . . well, before I get into that, did you ever write any of these research instrumentation grants where, you know, you're asking for money to help buy a piece of equipment? There seem to be, especially in the Gross lab where they are able to go to NIH [. . .] and get funds for instrumentation?

WATSON: Yes, we did that, and we also tapped the DOE [Department of Energy]. Michigan State is especially rich in plant science and DOE had an interest in the plant research projects and they had an instrumentation request for proposals, and it was in that context I spent most of the Christmas vacation break in about 1997, writing a grant that turned out to be one of the largest grants ever made by DOE to a university. We used those funds to purchase the JEOL double-focusing mass spectrometer which was high-resolution and good for exact mass measurements and had a FAB source and a collision cell for collision-activated association.

GRAYSON: You're doing some MS-MS work?

WATSON: Yes. **<T: 30 min>**

GRAYSON: [Yes], I guess that's a problem or a requirement and should be able to write these instrumentation grants and get support for buying equipment. Most equipment, I guess, has run in the million-dollar range now.

WATSON: Oh [yes], it's bad.

GRAYSON: Money is getting harder and harder to get from the government. Now, you had a lot of activity or involvement in a fraternity when you were an undergraduate, but you also were involved in the professional society . . . well, I guess ACS and ASMS in your professional career.[24] You said you were on the board of ASMS for—

WATSON: A year or so, I guess.

GRAYSON: [You were a] member at large?

WATSON: Correct, I was member at large and I . . .

GRAYSON: How was that experience?

WATSON: ASMS is a . . . I've seen it grow from . . . my first meeting was with the E14 part of ASTM [American Society of Testing and Materials] in [1964]. It was in McGill University in Montreal, [Quebec]. There were two hundred people at the whole meeting and—

GRAYSON: What, one oral session?

WATSON: I think so. I think that's right, no competition.

[24] Professor Watson served as Professor in charge of the ACS Short Courses on Mass Spectrometry from 1977-2006, and he was a member of the ACS Awards Committee from 1997-2000. He also served as ASMS Member-at-Large from 1980-1982; Chair of the Nominating Committee, 1983-1985; Program Co-Chair of the Sanibel Conference from 2000-2001; and member of the Education Committee from 2004-2006.

GRAYSON: [Yes.] Now it's what?

WATSON: Five or six thousand.

GRAYSON: Too many multiple sessions than you keep up with. It's ridiculous.

WATSON: Well, but that's thankfully mitigated to some extent by this webcast program that they have, which combines the video with the audio and makes it available on-line to attendees. A very valuable service.

GRAYSON: [Yes], well, you know, I mean they've got to do something because there's so much of interest going on in the—

WATSON: [Yes], in parallel.

GRAYSON: In parallel it's just . . . . And I think, did you serve any other positions with ASMS?

WATSON: No.

GRAYSON: And nowadays member at large has kind of a specific focus point.

WATSON: [Yes.] I was just . . . Burnaby Munson was the president, and I just did what needed to be done at his disposal.[25] I think I did something silly like salary survey or something but I guess that seemed to be of interest to the membership.

GRAYSON: And your ACS activities are primarily on the short course on mass spec, right?

WATSON: Yes.

[25] Burnaby Munson, interview by Michael A. Grayson at the University of Delaware, Newark, Delaware, 9 April 2010 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript # 0688).

GRAYSON: You never got involved in the more political aspects of the American Chemical Society?

WATSON: No.

GRAYSON: I wish the meetings weren't so expensive. I mean ASMS is really nice because it's affordable.

WATSON: [Yes].

GRAYSON: Did you develop any instrumentation that would go beyond, you know, the lab into something that might be marketed or patented?

WATSON: No.

GRAYSON: So that was—

WATSON: I guess the separator was the closest thing, but we were advised that there wouldn't be a big enough market to make it worth patenting.

GRAYSON: That's always the story.

WATSON: So that's okay with me.

GRAYSON: [Yes], well, it's another big basic piece of paperwork.

WATSON: [Yes], that's a good point.

GRAYSON: Analytical chemistry is a, kind of, a discipline that's going by the by in a lot of schools these days. It's <**T: 35 min**> looked down on, I think, to a certain extent and was there actually a program in analytical chemistry at Michigan State?

WATSON: Yes.

GRAYSON: Okay. Do they still have that going?

WATSON: Yes.

GRAYSON: Because I know a lot of schools kind of . . . . Well, but I guess MIT moved away from their analytical chemistry.

WATSON: I think that's right.

GRAYSON: I mean, I was kind of surprised when Biemann left, that the lab was disbanded. It seemed like I guess that they didn't want to?

WATSON: [Yes]. That was a strange situation, but I think Cathy [Catherine E. Costello] took most of the equipment over to BU [Boston University].

GRAYSON: [Yes]. I mean, that was a good move for her and for mass spec is just . . . I guess MIT just figured they didn't want to deal with it anymore. Well, I mean, things change.

WATSON: [Yes], I don't know the details but I suspect you're right.

GRAYSON: But the thing that always amazes me as I've mentioned before in some other interviews is in analytical chemistry sometimes people look down on that as a discipline but if we can tell the synthetic chemists, if he doesn't know what he's got, what he made, he can't figure out what . . . if he can't have some method of proving that, you know, analyzing it in a way that would unequivocally demonstrate what he made it seems like he's kind of out of luck. They accept the fact that they can get this information as just part of life, you know, it's like the regular routine, but analytical chemists made it happen . . .

WATSON: [Yes], that's a good point.

GRAYSON: They should get a little more respect. So you say they still do have an active program in analytical chemistry in Michigan State?

WATSON: Yes.

GRAYSON: That's good. I think, well, Purdue does still. And I guess all of the places that have research resources probably have a strong analytical chemistry [program]. Now we talked about some of these people. I was going to try to touch base with you on that. Douglas Gage, he mentored you somewhere along the way. Is that correct or did I get it confused? [. . .] Was he a mentor?

WATSON: No. He was a postdoc in the plant science part of Michigan State and was interested and used our facilities and proved himself to be quite knowledgeable in the interpretation of mass spectral data for his purpose. So when we needed a manager to replace Brian Musselman, we offered Doug the opportunity to join us as service manager, so to speak, as Doug had a good rapport with the users and became a collaborator effectively with them. Doug has a strong background in metabolism, especially as it applies to plants, so he was a valuable resource to those users as well as a representative of the mass spectrometry facility at the MSU. It was a good symbiotic relationship, so to speak.

GRAYSON: You did some work with Brian Sweetman at Vanderbilt as I recall.

WATSON: [. . .] Yes, well, Brian was a postdoc with me at Vanderbilt . . .

GRAYSON: Still in the clinical aspect of pharmacology?

WATSON: I guess. I think Brian remained as part of the prostaglandin analysis quantitation program.

GRAYSON: Oh [yes], prostaglandin, that was a part of a big scene there. **<T: 40 min>**

WATSON: [Yes], I've lost track of Brian.

GRAYSON: [Yes], well, there's a lot of people that you interact with over time. I think we talked about John Allison. He was at Michigan State, right?

WATSON: [Yes], well, he's no longer at Michigan State. He left about five years ago, and he's at The College of New Jersey, out on the East Coast and he's heavily into forensic applications of mass spectrometry.

GRAYSON: That's interesting. A CSI guy?

WATSON: [Yes], he had some interesting ideas about using MALDI to assess ink used by various ballpoint pens and so forth. He identified an oxidation product of the ink that accumulated as a function of time so that one could determine the age basically of certain documents that had been signed.[26] It was very clever.

GRAYSON: [Yes]. That could be important in like a document that's supposed to be signed ten years ago but it turned out it was signed ten days ago.

WATSON: [Yes]. John is a good scientist. He was a physical chemist before he came to Michigan State and was a good colleague.

GRAYSON: There's another name that seems to come from the past when I see it. It's John [F.] Holland.

WATSON: Oh, Jack Holland, [yes].

GRAYSON: [. . .] So what was your collaboration or involvement?

WATSON: Well, he and I basically ran the mass spec facility. I was the director and he was co-director, and he was a valuable colleague, a great consultant for both managerial problems or managerial issues with personnel and in terms of computing and developing means of rapid data acquisition. His main contribution to the center grant was the conception of an integrated transient recorder allowing us to use a time-of-flight mass spectrometer to collect rapid

[26]Donna M. Grim, Jay Siegel, and John Allison. "Evaluation of desorption/ionization mass spectrometric methods in the forensic applications of the analysis of inks on paper." *Journal of Forensic Sciences* 46, no. 6 (2001): 1411-1420.

acquisition of complete spectra; sets that one could acquire several hundred mass spectra per second and that's now been commercialized in part by [the LECO Corporation] over in [St. Joseph, Michigan].[27]

GRAYSON: [. . .] So that raises an interesting question. That is this whole period of your career when computers came from little clunky boxes with 16k of memory to really powerful tools. What was the first computer you had dedicated to a mass spectrometer? I mean, it didn't come with your LKB-9000, did it?

WATSON: No. It did not but soon thereafter we had gotten the PDP-12. [It] was dedicated to . . . well, in fact, we did use it on the LKB, it seems to me I recall but <**T: 45 min**> it was more readily amenable to the quadrupole instruments that we had.

GRAYSON: [Yes]. There's a company that flourished and then withered away totally.

WATSON: Digital Equipment Corporation.[28]

GRAYSON: I mean, they were the top dog in a mini, small computer business.

WATSON: That's right, you know, that's a good point. I hadn't thought about that.

GRAYSON: Somehow they missed the boat once the PC [personal computer] came.

WATSON: Is that what it was?

GRAYSON: Well, it seemed like they were trying to compete with . . . when Apple and IBM came out with their personal computers and **t**hey tried to compete in that market, and they failed and then the whole mini-computer thing for some reason or other just totally evaporated.

I was using PDP equipment at Wash U [Washington University] that was years old, and we had some Data General equipment on the old MS-50 but those were . . . that style of computing kind of just evaporated, disappeared or it was kind of like stuck between a big

[27] John F. Holland, Christie G. Enke, Michael R. Davenport, and Lawrence W. Janow. "Integrating transient recorder apparatus for time array detection in time-of-flight mass spectrometry." U.S. Patent 5,367,162, issued November 22, 1994.
[28] Digital Equipment Corporation was bought by Compaq in 1998 which merged with Hewlett-Packard in 2002.

computing center computer and a small personal computer and that the little middle ground just came out from under them because . . .[29]

WATSON: Pinched.

GRAYSON: [Yes]. Now your personal computer has got as much memory as . . . more memory than those old-style centralized big computer facilities. So then you were able to take advantage of the computer revolution in data acquisition and analysis?

WATSON: Yes, one of our main projects in the center grant was this use of this integrating transient recorder to accumulate full mass range spectra at a very rapid rate.

GRAYSON: This was off time-of-flight, I guess?

WATSON: Correct.

GRAYSON: And you're gearing up to go commercial with . . .

WATSON: We called it time array detection. [. . .]

[END OF AUDIO, FILE 1.3]

[END OF INTERVIEW]

[29] Data General, founded by three former Digital Equipment Corporation employees in 1968, was one of the first minicomputer manufacturers. The company was acquired by EMC in 1999.

INTERVIEWEE: **J. Throck Watson**

INTERVIEWER: **Michael A. Grayson**

LOCATION: **Watson's home**
Laingsburg, Michigan

DATE: **28 October 2013**

GRAYSON: [. . .] All right. So we're going to pick up the last . . . . You say you couldn't remember the name of the glassblower that you bribed with a bottle of Jack Daniels?

WATSON: I'm afraid that's right.

GRAYSON: Well, that's too bad because, you know, this guy made you famous.

WATSON: [Yes]. [laughter] Well, I guess you're right about that. [. . .] I'll just have to find out, and it could be that even Paul Vourus would remember because we used to have the glassblower come down to the wind tent every time we wanted to change some aspect of the . . . because the wind tent had some flanges but they were mostly glass pieces coming through the flange and that had to be modified from time to time.

GRAYSON: Well, then what about this—your name?

WATSON: My middle name is Throck.

GRAYSON: For a long time, I mean, I think when we first met, you went by Throck.

WATSON: Well, that's because I felt obliged to use it because I had used it. But my attempts to find out the origin have been disappointing. My mother claims that it was my father who came up with the name and there's no family history, there's no family meaning to the name Throck. [It was] simply something that my father had seen over the years and I got nabbed with it and I was always embarrassed by it, so I never divulged in grade school what T stood for. I think one time when pushed I said, "Tom." So I learned to lie at an early age. [laughter]

Well, when I got to college and began to recognize that uniqueness was a virtue, I began to appreciate the fact that I had a unique middle name and my mother had actually encouraged me to use it with my initial J. She didn't want me to have a nickname, so she christened me Jack, not John. So I'm christened Jack Throck Watson, and she wanted me to go by J. Throck Watson and I thought that was a neat idea and it was a fun name on which to develop a signature.

And then of course I had to declare what I wanted to be called and I solved the difficulty that especially Europeans had with pronouncing Throck, the t-h problem, so I backed off to Jack in deference to them in large measure. But many of my close friends affectionately picked up on **<T: 05 min>** Throck and still call me Throck, including Michael Grayson. [laughter] And my close friend, John Deutch who has become so famous, he calls me Throck.

I guess I've never really known the protocol, but I suppose the protocol is that those people who [. . .] who use their middle name in their signature actually use that name by which to be addressed. So I tried that from time to time and of course this all came across as being ambivalent and Burnaby Munson once told me that I didn't know who I was and I guess he was probably right. So I apologize for the ambivalence. but it's a name I've come to appreciate and of course it's my pen name and so I'm going to stay with it.

GRAYSON: Now your publications come out as J.T. Watson and [. . .] it's hard to track your record using standard, you know . . .

WATSON: Indeed, so I apologize for that and Klaus Biemann tried to straighten me out on that early on, I know. But I was still struggling with what to do. [. . .] It's unsettled.

GRAYSON: [Yes], obviously it is. I was, kind of, curious just because you know—

WATSON: And it's a curiosity for certain and it's a uniqueness that I've come to own—

GRAYSON: Someone who doesn't know who he is.

WATSON: Well, that's good. [Yes], that's a shame.

GRAYSON: So we were talking earlier about you left Michigan State around when? Sixty-four, sixty-five [years old]?

WATSON: [. . .] So I retired in 2006. So if you want to . . . just subtract 1939 from that and tell me how old I was.

GRAYSON: Sixty-seven.

WATSON: Really?

GRAYSON: So they didn't have a mandatory . . .

WATSON: No.

GRAYSON: Well, some places do, and it gets a little nasty.

WATSON: [Yes]. I mean so long as you have funds you can stay there as [professor] emeritus. They'll probably give you space. [. . .]

GRAYSON: [What] made you decide to retire?

WATSON: Well, I guess what brought it to the fore was funding. I had a renewal at about, let's say 2005 or something, and I thought I was doing pretty well and so I just decided, "Well, I'll give it one more shot and if I make it, I'll continue to have fun in the lab," and I was having fun. I had [an] excellent postdoc and I still had a couple of senior graduate students who were excellent. So I did the renewal and submitted it to the study section that had found the previous grant outstanding. I had a dozen or so publications; I thought I was doing okay. What I didn't know was the study section had been heavily transformed from a panel of protein chemists using a variety of analytical techniques **<T: 10 min>** to a panel that was almost exclusively x-ray crystallographers who summarily trumped or triaged my grant application and allowed me to exercise one of my two options that I had designed for myself upon submitting the grant; namely that I would either take the money and run or if I didn't get funded, I would go fishing, so I went fishing. I had a wonderful time in Northern Ontario, [Canada], Wilderness Lake. Fly in with my brother and cousin—wonderful time, shore lunch, walleye over a campfire. Caught a forty-two-inch northern pike on eight-pound test line with no steel leader—not a small accomplishment. Do you do any fishing?

GRAYSON: I'm not a sportsman. I like being in the woods and hiking, but I've never caught anything.

WATSON: Oh, so you don't understand what northern pike means? It's like hanging onto an alligator. I mean, these things are vicious.

GRAYSON: It's a challenge?

WATSON: Oh, unbelievable.

GRAYSON: But a kind of a neat switch in careers that, you know, have the science career and do some work on things.

WATSON: [Yes], well, I had many more fun things on my list that are curtailed.

GRAYSON: [Yes], unfortunately. I was looking at your publication list and I saw a name, a phrase: "to netcrawl." MRSA, did you guys do any work with . . . MRSA is some kind of super bad project.

WATSON: I don't know. I don't understand what you're talking about.

GRAYSON: MRSA? It's an antibiotic-resistant bug that I thought I saw . . .

WATSON: I don't know, I don't remember this. [. . .]

GRAYSON: So what do you think is your most important publication or most important ones of your publications, or do you have any feelings for any of these?

WATSON: Oh, well, I think the one that I'm most proud of is the one where I lay out the cyanylation of cleavage, mass analysis of cleavage products to define the connectivity of cysteines in a disulfide-bonded protein.

GRAYSON: That's a fairly recent one, I guess.

WATSON: Yes. I think the principal author name is Wu.[30]

GRAYSON: Okay.

WATSON: Are you looking at it?

GRAYSON: I'm looking at a list of . . . I did an analysis of your "high citation" publications **<T: 15 min>** and I'm looking to see if Wu . . . . And I see a: Wu, "A novel technology for cyanodisulfide carriers in proteins."

WATSON: [Yes], there you go.

GRAYSON: 1997, okay.

WATSON: That sounds right. It's published in what, *Protein Science*? Or *Analytical Chemistry*.[31]

GRAYSON: Wu, it is published in *Protein Science*. "Novel method of describing cyanic oxides and disulfide bonds in proteins and . . . ." Okay, so that is one of the ones that I have listed in my selection of items. [. . .]

WATSON: Well, see I have never used that algorithm. I have never done a search. I have never done whatever the hell it was you did to do that. So how does that rank?

GRAYSON: Among your papers?

WATSON: [Yes], that is to say it being cited one hundred ninety-seven times.

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[30] Jiang Wu and J. Throck Watson. "A novel methodology for assignment of disulfide bond pairings in proteins." *Protein Science* 6, no. 2 (1997): 391-398.

[31] Jiang Wu and J. Throck Watson. "Optimization of the cleavage reaction for cyanylated cysteinyl proteins for efficient and simplified mass mapping." *Analytical Biochemistry* 258, no. 2 (1998): 268-276.

GRAYSON: One hundred seventeen.

WATSON: Is that good?

GRAYSON: Well, [yes], for a recent paper. Most papers, probably they're only cited more than half a dozen times, if that much.

WATSON: Well, see, I didn't know that even. It's pretty embarrassing. You know, when I was writing the fourth edition, I was fairly expert with the electronic libraries. I mean, I knew how to use [. . .] PubMed, and I knew how to use SciFind, SciFinder. And [. . .] I felt so in control and I had good bibliographies in that there are good bibliographies in that fourth edition.

GRAYSON: [Yes], they are. I was looking at it. It's pretty thorough. And that's important but I'll tell you the thing that I find quite interesting. If you think about this, this business of being able to keep track of citations has only been a recent development. So papers published before about 1995 or 1990, and everything published after that period, somewhere in that range the citations—

WATSON: Dropped substantially?

GRAYSON: Are electronic. No, they're electronically monitored automatically, okay. If you publish, let's say . . . let me put it this way: you publish a paper in 1970 that got a hundred citations, it might show up with ten because it would only show up in the modern record by people who cited it in the last couple of years.

WATSON: I see.

GRAYSON: And if people cited it in 1971 or '72 or '73 or '74, that would never show up because that's—

WATSON: Out of the window?

GRAYSON: Well, it's out of the window of electronic tracking cites.

WATSON: Is that right?

GRAYSON: [Yes]. So I mean in other words—

WATSON: I don't . . . [yes], I didn't know this.

GRAYSON: [Yes], but what's impressive to me is this paper you published in [. . .] 1978.

WATSON: What was that?

GRAYSON: "Effects of caffeine on plasma renin activity, catecholamines and blood pressure."[32] [. . .] This has one hundred twenty-one cites, but this was a paper that's published in 1978 which means . . . the fact it has one hundred twenty-one cites, it means a lot of people have been citing it in the last ten or fifteen years. So it's got some survivability.

WATSON: I see.

GRAYSON: I don't know whether or not that means anything. Or there's something special about that.

WATSON: [Yes], that was a kid **<T: 20 min>** at Vanderbilt. It's interesting. I don't know what the hell I did to deserve being on that thing.

GRAYSON: Now the other early paper is 1975: "Urinary prostaglandins. Identification and origin."[33] That was cited forty-eight times. But now you say that's been cited forty-eight times in the last ten years, so it doesn't count all the other citations that occurred from 1975 until 1995.

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[32] David Robertson, Jürgen C. Frölich, R. Keith Carr, J. Throck Watson, John W. Hollifield, David G. Shand, and John A. Oates. "Effects of caffeine on plasma renin activity, catecholamines and blood pressure." *New England Journal of Medicine* 298, no. 4 (1978): 181-186.

[33] J. C. Frölich, Thomas W. Wilson, Brian J. Sweetman, Murray Smigel, Alan S. Nies, Keith Carr, J. Throck Watson, and John A. Oates. "Urinary prostaglandins. Identification and origin." *Journal of Clinical Investigation* 55, no. 4 (1975): 763.

WATSON: So this is a good time to tell me the same thing again, I suppose, and that is t the earlier it was published, the more significant is the number of citations or something?

GRAYSON: [Yes], because it shows the fact that that old paper is still being cited today. Because the only way we know that it's being cited that frequently is because it's only in the last ten years or so that the ACS is able to actually track all the citations of papers electronically. I mean, as you are aware like with EndNote, managing this stuff is a lot easier, you know, with a computer. So it's easy. It's easy for a paper that's published today, to electronically find out all the different papers that were cited in that paper that was published.

So when you published this paper in '75 there was no easy way to find out how many times that paper was cited unless some person looks at the literature in its total entirety and finds out how many cites there were that . . . . Do you understand what I'm saying?

WATSON: No.

GRAYSON: Well, an old paper cited frequently means it's still being cited by people today, regardless of how many people may have cited it before, which we don't know. It's a way of – for me to try and dig into the meat of your research and what it is that . . . this says what people thought was important about your research, okay?

WATSON: [Yes], I guess so.

GRAYSON: I mean, things that you did a long time ago, they're still being cited; [that] means there's something classic to that paper. Something that people find important.

WATSON: Yes. [. . .] And how do you distinguish those again? What's the criterion?

GRAYSON: SciFinder. [. . .] SciFinder today—and as much as the ACS was in *Chemical Abstracts*—for every paper that is in SciFinder or in the *Chem Abstracts*, they track down [. . .] how many papers are cited in that publication and then they do the math. And when I come in here—which I use SciFinder—I search on, "Watson, J. Throck. J.T. J." whatever it is. [. . .] And I can then, when I get that list of publications, I can arrange that list according to the number of citations that were made to each of those papers and then I use that information to try and gain

some insight into what was significant about the body of work. So, the most highly-cited paper is 195 cites, published in 1987: "Novel fragmentation process of peptide . . ."[34]

WATSON: And is Biemann in on that one or is that just Stults and me?

GRAYSON: [. . .] Did you collaborate with him on that?

WATSON: [Yes]. Stults found this interesting sequence which Klaus had also latched onto and was calling them the W ions.

GRAYSON: Oh [yes].

WATSON: And so we finally . . . I called him up and said, "Look, we're thinking about publishing this." And he said, "Well—" He says he'd been working on it **<T: 25 min>** already. **S**o we finally decided to do something jointly.

GRAYSON: Okay, then we need to do a search.

WATSON: And Biemann is the principal author.

GRAYSON: I'm going to check that. [. . .] Oh [yes], here it is: Stults, John and Watson, J. Throck, and it's a 1987 paper.[35]

WATSON: Was that an *OMS* [*Organic Mass Spectrometry*] paper or *BEMS* [*Biomedical Environmental Mass Spectrometry*]?[36]

GRAYSON: *Biomedical Environmental Mass Spectrometry*.

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[34] Richard S. Johnson, Stephen A. Martin, Klaus Biemann, John T. Stults, and J. Throck Watson. "Novel fragmentation process of peptides by collision-induced decomposition in a tandem mass spectrometer: differentiation of leucine and isoleucine." *Analytical Chemistry* 59, no. 21 (1987): 2621-2625.

[35] John T. Stults, and J. Throck Watson. "Identification of a new type of fragment ion in the collisional activation spectra of peptides allows leucine/isoleucine differentiation." *Biomedical & Environmental Mass Spectrometry* 14, no. 10 (1987): 583-586.

[36] There was also an *OMS* paper from this period: Brian D. Musselman, J. Throck Watson, and Chi K. Chang. "Direct evidence for preformed ions of porphyrins in the solvent matrix for fast atom bombardment mass spectrometry." *Organic Mass Spectrometry* 21, no. 4 (1986): 215-219.

WATSON: Oh, that's too bad, [yes].

GRAYSON: So, Klaus is not listed on that one. [. . .] So, you already told me what you thought was your most important paper which I think is listed amongst those that I was able to find and I just was looking at obviously how people see the body of your work. Tells me something about what's important in it.

WATSON: Okay. So the answer to that point is that it was the isoleucine-leucine thing was.[37]

GRAYSON: That's one that you said and that's one of the ones that was most highly cited.

WATSON: [Yes], so statistically that one stands out. That was important. There's the so-called W ions—oh man, I used to know how that worked!

GRAYSON: Well, do you have any kind of a wrap-up? I mean, [. . .] what do you think is important to the future vitality of—

WATSON: Oh shit, I don't know.

GRAYSON: Research and development influence or a message to the future, so to speak?

WATSON: I don't have any. I'm not good at that.

GRAYSON: Not a good prognosticator?

WATSON: I'm not. [. . .] I'm not a visionary.

GRAYSON: So, ah, I do have one other question, and I noticed while I've been here that there's several copies—small pamphlet copies—of the Constitution of the United States lying around. And I was wondering if you were a constitution scholar in your retirement?

[37] Johnson, Martin, Biemann, Stults, and Watson. "Novel fragmentation process of peptides."

WATSON: No. I just open my mailbox.

GRAYSON: Oh, okay. This is stuff that comes in the mail?

WATSON: [Yes].

GRAYSON: [. . .] Well, unless you have any other comments or things you want to say I'm going to wrap this puppy up and you can get back to enjoying your retirement here.

WATSON: Oh geez, Mike, well, I've got to tell you I'm certainly flattered by this whole process by being considered to say something worthwhile and I can't. [. . .]

[END OF AUDIO, FILE 2.1]

[END OF INTERVIEW]